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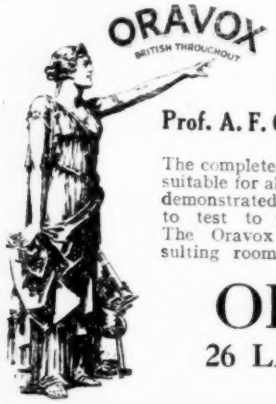

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LECTURE III.*

LOCAL VASODILATOR REACTIONS.—HISTAMINE (*cont.*).—ACETYL CHOLINE.—CONCLUSION.

Histamine: Its Significance in Certain Pathological Reactions.

IT is, I think, in the field of the abnormal, pathological reactions of minute blood-vessels, and of certain tracts of involuntary muscle, that the greatest change and clarification of our conceptions is effected by the definite knowledge now available concerning the normal presence of histamine in so large a proportion of the cells of the body, and the ease with which it is liberated by injury of their protoplasm.

Anaphylactic and Allergic Reactions.

At the time when the activity of histamine was newly discovered and under investigation, the rediscovery of experimental anaphylaxis in the guinea-pig, and the dramatically fatal character of the shock in that species, had aroused fresh interest in the physiological details of the reaction, as seen, with such remarkable superficial differences, in different animal types. The knowledge was then new, that an artificial product of protein digestion, the familiar "Witte's peptone," when injected into a vein of the normal dog and of the normal guinea-pig, reproduced in each the characteristic and contrasted symptoms of the anaphylactic shock; in the dog, the tensely congested liver, hæmorrhagic intestinal mucosa, collapse of the circulation; in the guinea-pig, asphyxiating contraction of the bronchioles, usually fatal before any pronounced direct effect on the circulation had shown itself (Biedl and Kraus).[1] It was natural, then, to suppose that the anaphylactic shock was due to liberation of a protein cleavage-product in the circulation, by digestion of the reinjected antigen When the action of so simple a substance as histamine was found to produce the principal features of the shock with their characteristic contrasts in the different species, it was again natural that it should be identified with this hypothetical, circulating anaphylatoxin by certain continental writers. To me the theory, in that form, never appealed. Certain features of the anaphylactic reaction, such as the loss of the coagulability of the blood and the multiple small subserous hæmorrhages, were missing from the effects of histamine but reproduced in the action of substances like the Witte peptone. Later the investigations of a number of observers, including my own, convinced me of the correctness of the view which attributed the symptoms of the anaphylactic reaction, not to the formation of a poison in the blood, but to the reaction between the antigen and a precipitating antibody located in the cell protoplasm (Dale).[2] This theory of cellular sensitisation still seems to me to fit the known facts of anaphylaxis, in its original sense of an acquired specific sensitiveness to a soluble antigen. On the other hand, it was clear that the location of the reaction in the cells did not exclude the formation of a poison by protein cleavage; this might take place in the cells, and might there, indeed, be more rapid and severe in its effects than if it occurred in the blood. Abel and Kubota[3] definitely suggested the intracellular formation of histamine, by protein digestion, as the cause of the anaphylactic symptoms, and as accounting for their similarity to those produced by histamine directly injected.

It seemed to me that such suggestions went beyond the known facts. There was, and there is still, no convincing evidence, either of an immediate protein digestion resulting from the union of antigen and antibody, or of the liberation of histamine itself in the enzymatic cleavage of proteins. I suggested, indeed, on the facts then available, that the puzzling resemblance between histamine effects and the symptoms seen in the anaphylactic reaction might as logically find its explanation in the reverse direction: the effects of histamine itself might conceivably be due to its producing such changes in the state of dispersion of the protoplasmic colloids, as could be assumed to take place in the intracellular union of antigen and antibody.

Our present knowledge seems to me to have rendered all such speculations superfluous and obsolete. Lewis, finding that a local anaphylactic reaction in the human skin presented the familiar "triple response" of the blood-vessels to a local injury, concluded that the union of antigen and antibody in the sensitised cells acted, like any other injurious stimulus, by releasing the preformed H-substance. Such a conception appears to me to fit all the known facts, and to make clear the meaning of many which were difficult to interpret on any other theory. It was difficult, on our earlier conceptions, to explain why, in each species, only those cells should apparently become sensitive to the foreign antigen, and react to its reinjection, which had normally a special sensitiveness to histamine. There is now no necessity for assuming such preferential sensitisation of the cells which participate in the overt reaction. Cells of other types may be assumed to contain the specific antibody, and, as the result of its union in their protoplasm with the foreign antigen, to liberate preformed histamine; but only those cells which, in each species, are sensitive to histamine will exhibit the physiological reaction to it. The effect thus produced, and constituting in each species the central symptoms which determine the general aspect of the anaphylactic shock, could arise in one of two ways. The histamine might be liberated from, or in the immediate neighbourhood of, the reacting cells; on the other hand, anaphylactic injury of the cells of some large organ, such as the liver, might liberate histamine into the general circulation in such quantity as to produce its effects in the body generally, and thereby to cause a histamine-response in cells which are not themselves sensitised to the antigen, but are reactive to histamine. These alternative processes can actually be traced as the central features in the shock, as seen in the guinea-pig, in the one case, and the dog in the other. In the guinea-pig, in which death is produced by contraction of the plain muscle of the bronchioles, isolated samples of plain muscle give a direct response to application of the antigen in high dilutions; the histamine, we must suppose, is liberated from, or in the immediate neighbourhood of, the reacting cells. Isolated plain muscle from the anaphylactic dog, on the other hand, gives no significant response to the antigen, and the blood-vessels in the perfused limb of such a dog are but weakly affected if the antigen is added to the perfusing fluid. Yet when the antigen is injected into the circulation of the whole anaphylactic dog there is a general vascular and plain-muscle reaction, strikingly similar to that produced by histamine. As Manwaring[5] first showed, and others have abundantly confirmed, the sensitisation of the dog to the antigen is almost limited to the cells of the liver. If this organ is completely excluded from the circulation, injection of the antigen into the blood stream has little or no effect, though histamine, under such conditions, produces its usual general effects on small blood-vessels and plain muscle. If the blood leaving the liver of an anaphylactic dog

* Lectures I. and II. appeared in THE LANCET of June 8th and 15th respectively.

is perfused through other organs of a second, normal dog, production of the anaphylactic shock in the first dog causes the vessels and plain muscle of the second to show responses such as they give to histamine. In the dog, therefore, the specific anaphylactic sensitisation by antibody chiefly affects the liver cells; when these are injured, by the immune reaction occurring in their protoplasm, histamine which we know them to contain, is released in such quantities as to produce its effects not only on the liver-vessels but on the histamine-sensitive cells of the body at large.

That these two types of reaction do occur in the guinea-pig and dog can hardly be doubted; but such actions of histamine, in the immediate neighbourhood of its release or distributed by the circulation, do not complete the picture of the anaphylactic reaction in either species. As I have already mentioned, the anaphylactic shock involves effects of a more injurious and lasting nature than any which direct injection of histamine can produce. A loss of the coagulability of the blood is a feature of the anaphylactic reaction in all species, but not of the reaction to histamine. It is an effect following acute injury of the liver cells by many poisons. The dog's liver, in the anaphylactic shock, becomes enormously distended with blood and lymph, the reaction being much more severe and persistent than that produced by the direct effect of histamine on the vessels of this organ. The injury, in other words, is a far more severe and disorganising one than would be necessary to produce a physiological release of histamine, and the loss of the coagulability of the blood would alone suffice to show that other constituents of the liver cells are in fact liberated. It is unlikely that the histamine, which the liver must pour into the general circulation under such conditions, will be free; it is more likely to be involved in colloidal complexes with the other cell constituents. Some of Manwaring's more recent experiments[6] suggest that such complexes involve the antigen, so that they are prevented, by some other kind of antibody, from producing the histamine action on other tissues of a dog which has been immunised to it; but the meaning of these observations is not yet perfectly clear.

The fact that in the guinea-pig, especially when death from the shock is delayed, the blood also shows a loss of clotting power, which histamine does not produce, may be taken as evidence that the liver is also involved in the injurious cellular reaction in this species. The occurrence of capillary hæmorrhages in the shock, which histamine again does not produce, may be taken to indicate that the vascular endothelium is itself sensitised to the antigen, and directly injured by the immunity reaction, in addition to being affected by release of histamine from other cells in its neighbourhood.

We may picture the anaphylactic shock, therefore, as the result of cellular injury, due to the intracellular reaction of the antigen with an aggregating antibody. Whether this is general, or localised in a particular organ, histamine will be released, and its effects will be prominent in the resulting reaction, imposing a general resemblance to the syndrome produced by histamine itself, on the symptoms seen in each species. The cell injury, however, is not limited to the degree required to produce a release of histamine, and involves other and more direct results. Such a conception is in accordance with all the facts as yet available, and it has the advantage of rendering intelligible, not only the striking resemblance between symptoms of the anaphylactic reaction and those produced by injecting histamine, but also the various and equally significant points of difference between the two syndromes.

Along precisely similiar lines we can explain the effects of the various "allergens" or "haptenes" on the subject of a natural or acquired idiosyncrasy. Whatever view be taken as to the similarities or differences between such conditions and artificial anaphylaxis, all certainly involve a condition of the cells such that a normally harmless substance is specifically injurious to them; in all cases the reaction to such specific injury involves symptoms like those produced by histamine, and for the reason that in all cases histamine is released by the injury.

Anaphylactoid Phenomena.

There is a large group of pathological reactions, some produced by natural infections and others by artificial injection of various substances into the blood stream in which groups of symptoms occur, more or less closely resembling those seen in the anaphylactic or allergic reactions. A large literature has grown up around the significance attributed to these resemblances. Intravenous injection into the guinea-pig of various chemically inert colloids and suspensions, with or without preliminary incubation with serum, produces symptoms showing a general similarity to those of the anaphylactic shock in that species. These facts have been used as the basis of more than one theory as to the cause of the symptoms of the anaphylactic reaction. When the symptom-complex is regarded as specific to anaphylaxis, the results of injecting some of these artificial mixtures are, indeed, so similar that the resemblance appears highly significant. When once it is realised, however, that any kind of general cell injury which leads to the release of intracellular histamine must be followed by symptoms of this type, this significance largely disappears. Hanzlik and Karsner[7] have surveyed the actions of a wide variety of agents, including organic colloids such as agar-agar at one end of the scale and ions of heavy metals at the other, the injection of which into the blood of the guinea-pig produces the "anaphylactoid" syndrome. It is perhaps significant that they find, as a common feature of the action of many of these, capillary embolism and thrombosis in the lungs. With the knowledge that lung tissue is peculiarly rich in histamine, and that the most prominent feature in the overt reaction of the guinea-pig to these varied substances is the closure of the bronchioles and consequent asphyxia, which histamine itself also produces in minute doses, it seems reasonable to look to the liberation of this substance from injured cells, of the lungs in particular, for that "common basis for the truly anaphylactic and the anaphylactoid reactions" in the guinea-pig, which Hanzlik and Karsner indicate as an aim of further investigation.

The matter, however, is not quite so simple as that. A number of chemically inert substances, when mixed and incubated with blood serum outside the body, impart to the latter the power of eliciting the anaphylactoid symptom-complex when injected intravenously. Such toxic serum does not itself contain histamine; it does not directly stimulate isolated plain muscle as histamine does; but from its effects when injected we obtain evidence of its directly injurious action on the blood cells and on the vascular endothelium (see Dale and Kellaway).[8] The effects, therefore, of injecting some of these foreign substances into the blood may be due to their direct mechanical injury of cells with which they come into contact, liberating histamine at various points by a process analogous to that causing Lewis's triple response of the skin vessels. Others, apparently by adsorbent action on the protein-lipoid complexes of the blood plasma, may cause these in turn to act as an injurious foreign substance, and may thus, at second remove, produce the histamine-liberating cellular injury. In the case of some substances, again, such as the artificial peptones, it may be difficult to decide to what extent they are acting directly, to what extent indirectly through cell injury. Witte's peptone, for example, has direct effects on plain muscle which suggest that it may contain histamine. The project of demonstrating the presence of that base in small proportions in such a complex mixture of peptides, by its actual isolation in a state of chemical purity, would, according to our experience with other materials, not be a very hopeful one. Short of this, Abel and his co-workers have put forward chemical evidence to justify the presumption of its presence. There are features of the action of such a peptone, however, which make it clear that this is not wholly due to histamine already present in it,

but at least in part to an injurious action on the liver cells, like that seen in the anaphylactic shock, with ensuing indirect effects on other organs, and possibly also with some direct injury of endothelial cells outside the liver.

When once it is realised that symptoms having much in common can be produced, either by injecting histamine itself directly, or by injecting injurious substances which will cause its release in the body, you will appreciate the difficulty of disentangling the different parts of the total effect, in the case of a preparation which may contain both histamine and such other substances. It must be borne in mind, also, that general endothelial injury by itself, apart from the effects of histamine incidentally released, would directly produce a circulatory collapse having at least points of similarity with that produced by a toxic dose of histamine; so that again, in the case of some substances such as poisonous metallic ions, injected intravenously, it may be very difficult to decide what part of the total effect should be attributed to direct, irreversible destruction of the tone of the minute vessels, and what part to the secondary pharmacodynamic action of histamine released by the general cell injury.

These various considerations appear to me only to reinforce the suggestion that the syndrome of the anaphylactic shock has no special relation to that condition, and that the appearance of that syndrome, or of any of its constituent symptoms, as the result of any other kind of artificial intervention or natural, pathological process, does not warrant the presumption of a causal relationship or common basis, except in so far as general or local cellular injury is present in each case. A group of symptoms common to all these reactions is that which histamine will produce; and the release of this substance, from cells injured by a multiplicity of agents, would satisfactorily account for this common element in their effects.

Limitations of the Significance of Histamine.

If you have so far followed my argument, you will not suspect me, however, of suggesting that the liberation of histamine will by itself account for *all* the symptoms included in the group of phenomena which we have been considering. The point is of such importance that, at the risk of repetition, I must make it with more directness and emphasis. We have no justification for assuming that histamine is the only cell constituent which injury liberates. It is possible to imagine an injury so mild in degree, and so restricted to cells not concerned in the ensuing reaction, that only histamine might be liberated, or only its effects be visible. More severe injury, however, whether physical or chemical, local or general, might be expected to introduce other elements into the reaction; we have seen that it does so in the anaphylactic and anaphylactoid reactions; and it may do this, either by causing liberation of other and unknown cell constituents, or by directly affecting the physiological integrity of the endothelium of the reacting vessels. We may not know, in any particular case, which of these possibilities is the more important; but we do know that a fully developed, local inflammatory reaction involves much that histamine cannot reproduce, in the wandering of white and the leakage of red cells into the injured tissue, the thrombosis, and the resulting arrest of the circulation. Histamine can satisfactorily account for the evanescent response to mild injury, and for the initial physiological phase of the response to injury more severe in degree. As the reaction becomes frankly pathological, the effects of histamine fail more and more to fill the picture.

I can imagine that in some minds, and particularly in those accustomed to the detailed study of pathological blood-vascular reactions, this failure of the effects of histamine to cover the whole field may raise doubts of its real significance. On my own mind, which views the phenomena instinctively from the angle of physiology and pharmacology, the effect of this limitation is in the opposite direction. If histamine reproduced all the reactions to any kind or degree of cell injury it might merely be one of innumerable cell poisons producing a common set of vascular reactions, by liberation of an H-substance having no chemical relationship to any of them. That the action of histamine is not thus directly injurious, but a specific, reversible pharmacodynamic action on certain contractile cells, on which it acts in extreme dilutions, is to me a strong argument for its true, physiological significance, and for its identification with Lewis's H-substance. Its normal occurrence in living cells has now been chemically demonstrated in a wide range of tissues, and can be legitimately inferred from physiological tests in many others. I think that we have sufficient evidence for regarding it as the physiological agent of the relaxation of the tone of the small blood-vessels in response to irritation or injury of the tissues, whether local or general. Whether it is also concerned in the more strictly physiological relaxation of the minute vessels, in response to metabolic activity, the future may show; as yet we have no evidence of such a function.

ACETYL-CHOLINE.

I ask your attention now to the action of an entirely different type of vasodilator substance, which resembles histamine in certain features of its scientific history. The simple quaternary ammonium-base, choline, has long been known as a constituent of the tissues, where it enters into the constitution of the group of phosphatide lipins known as lecithins. Possessing an alcoholic hydroxyl, it can be esterified, and its acetic ester, acetyl-choline, was prepared by Nothnagel in 1894.[9] Like histamine, therefore, it was made in the chemical laboratory long before it acquired a physiological interest. Choline was already known to produce a depressor effect on injection into the mammalian circulation, when Reid Hunt and Taveau,[10] in 1906, observed that acetyl-choline produced the same kind of effect in about one-thousandth part of the dose. It had a choline-like action, but was a thousand times, or more, as active. Hunt and Taveau speculated on the possibility that such a substance might occur in the body, but found no evidence of it. At this stage they regarded its action as due to weakening of the heart-beat. My own interest in it[11] was first aroused, again as in the case of histamine, by the discovery of its presence in certain extracts of ergot, from which my colleague Dr. Ewins succeeded in isolating it.[12] On making a more systematic investigation of its actions on various organs, I was struck by the remarkable parallelism between its effects and those produced by stimulation of parasympathetic nerves. It showed an extraordinary instability when injected into the blood stream, presumably being hydrolysed with the liberation of the relatively inactive choline. Accordingly its parasympathetic effects were even more rapidly evanescent, as well as more powerful, than the sympathetic effects of adrenaline produced under like conditions. A striking feature of its action, and one in which the correspondence with parasympathetic effects appeared to fail, was the general dilatation of small arteries, produced by almost incredibly minute doses of this substance, not only in the areas receiving vasodilator fibres from parasympathetic nerves, but in organs such as the limbs, where the only known vasodilator nerve-supply to the arterioles was, and still is, that of the antidromic, axon-reflex mechanism of the sensory nerves. When Reid Hunt,[13] a few years later, confirmed this observation, of the predominantly vasodilator nature of the depressor effect of acetyl-choline in minute doses, he was struck with the resemblance, in character and distribution, between its effects on limb vessels and those produced by peripheral stimulation of the appropriate sensory nerve-roots. He was inhibited, however, from attributing any significance to the resemblance, by the observation that the effects of acetyl-choline were completely abolished by doses of atropine which left the antidromic effects unimpaired.

During more recent years the activity of acetyl-choline has gained interest in several directions. I had observed that, apart from its parasympathetic and vasodilator effects in minute doses, readily annulled

by atropine, acetyl-choline, injected in larger doses after atropine, exhibited, like many other quaternary ammonium bases, a powerful nicotine-like action on ganglion-cells. This second aspect of the action of acetyl-choline has been found to extend to the production also of certain peculiar motor effects on voluntary muscle, which nicotine was already known to produce. Langley[14] had studied the slowly developed tonic contractions of frog's muscle, produced by applying nicotine, and Riesser[15] found that immersion of the muscle in dilute solutions of acetyl-choline produced similar effects. Heidenhain[16] had observed that the voluntary muscle of the dog's tongue, when deprived by degeneration of its motor fibres from the hypoglossal nerve, responded by a slow wave of contraction—he called it a " pseudomotor reaction "—to injection of nicotine into the circulation. Frank, Nothmann and Hirsch-Kauffmann[17] found that acetyl-choline, in relatively small doses, produced this contraction of the denervated tongue in a very striking form, and that other voluntary muscles, such as those of the limbs, became similarly responsive to acetyl-choline when deprived of their motor nerves. There was a tendency to speculate on these actions of acetyl-choline on voluntary muscle as implying a parasympathetic motor innervation, connected with tonus, in addition to the ordinary motor nerve-supply. Gasser and I,[18] however, were able to show, I think convincingly, that these effects of acetyl-choline on voluntary muscle were not directly related to its parasympathetic action, but were entirely concerned with that other aspect of its activity, which it shares with substances like nicotine.

Chemical Transmission of Parasympathetic Effects.

Two other lines of evidence which have lent new interest to the action of acetyl-choline concern its parasympathetic effects. Weiland,[19] working in the laboratory of the late Prof. Magnus in Utrecht, found that an isolated, sealed loop of rabbit's intestine, suspended in Ringer's solution, gave up to the latter a substance which stimulated rhythmic activity, when added to the solution in which another loop was suspended. Le Heux,[20] in the same laboratory, investigated the chemical nature of this substance, and succeeded in isolating choline. Testing the stimulating effects of pure choline on such isolated pieces of intestine, he found that it was greatly intensified if the warm saline solution, in which the tissue was suspended, contained acetates. He was led to suggest the formation of acetyl-choline in the tissue as a preliminary to the action of choline. In the same connexion we may note an observation made by Hoet[21] on the activity of such isolated loops of intestine. Magnus had found that part of the automatic rhythm of such a preparation was stopped by atropine, and had attributed it to choline. Hoet found that if, after the animal had been killed, but before the loop was detached from its natural connexions, the vagus nerve was strongly stimulated, this atropine-sensitive element in the rhythm of the subsequently isolated loop was much increased.

The clearest evidence, however, of the peripheral release, during stimulation of the vagus, of a chemical substance transmitting the characteristic effects of vagus impulses, has been provided by the work of Otto Loewi[22] and his co-workers on the frog's heart, and of others who have repeated and confirmed their results. In a series of publications from 1921 onwards they have built up an imposing structure of evidence, for the details of which the original papers must be consulted. Here I can only give the story in outline. Briefly, it has been shown that when an isolated frog's heart, containing a small volume of Ringer's solution, is subjected to inhibition by stimulation of the vagus nerves, a substance passes into the Ringer's solution which, on transference to another isolated heart, reproduces there the effects of vagus inhibition. In passing it may be noted that Loewi found, and others have confirmed the finding, that when the action of the sympathetic accelerator fibres in the vagus prevails, so that a stimulation of the rhythm replaces inhibition, an accelerator substance passes into the Ringer's solution. For the present, however, our concern is with the inhibitory vagus-substance and its properties. The quantities are minute, but the behaviour has been examined with great ingenuity. The substance is not free choline, though choline is present; for acetylation increases the activity, but not in nearly so high a proportion as it does that of pure choline. The activity of the " vagus-substance " can be annulled by treatment with a tissue esterase, and then not merely restored by acetylation, but increased beyond the original level.

Looking at the whole of the evidence, one fails to find any point of it which is incompatible with the supposition that the vagus substance is, indeed, a highly unstable and intensely active choline ester closely resembling acetyl-choline in its properties. The instability of such a substance would lead to the liberation of some free choline; so that, even if the substance were acetyl-choline itself, complete acetylation of the mixed residue would lead to the increase of activity in varying proportion, which is actually observed. The muscle of the frog's heart yields a similar substance to artificial extraction, even without vagus inhibition; but vagus inhibition, as a preliminary to extraction, increases the yield.

It should be noted that somewhat similar observations were made, many years before this recent series, on the mammalian heart. Dixon [23] observed in 1906 that the mammalian heart yielded to extraction a substance soluble in alcohol, and producing a muscarine-like inhibition when applied to the heart of a frog, and that the yield was greatly increased by stimulating the vagus up to the moment of extraction. The action of acetyl-choline was not then known, and Dixon's observation was not chemically developed. Later, with Hamill,[24] he gave a wider application to the conception, but no further evidence directly concerned with vagus action. A few years ago Plattner [25] made experiments of a similar kind, and, with the knowledge before him of the behaviour of Loewi's substance from the frog's heart, was able to obtain evidence of the presence of a similar substance in the mammalian heart, behaving like a choline ester, and increased during vagal inhibition.

Acetyl-Choline a Normal Constituent of the Body.

Altogether, then, there appeared to be a good body of evidence in favour of the view that the vagus produces its effects, not by direct passage of its impulses to the effector cells, but by liberation in relation to them of a substance having the effects associated with stimulation of the vagus, and in other respects having the properties of an unstable choline ester. Of the extensive series of choline esters which have hitherto been examined acetyl-choline stood out as unique in the possession of properties which would fit it for the rôle of the vagus substance. The temptation to assume the identification must have been experienced by many interested in this field of work. The chemical isolation and identification of the actual vagus substance, from minimal traces of material, was clearly not to be expected. To me it seemed that the one piece of evidence needed to justify such an assumption, and yet not wholly beyond credible attainment, was the discovery, in some organ of the normal animal body, of a substance having these physiological properties, its isolation and chemical identification. Less than a year ago the opportunity was presented to my colleagues and myself by a chance observation. In completion of our series of investigations on the distribution of histamine we were working on spleen extracts, using the spleens from freshly killed oxen and horses. Histamine was in due course isolated, in quantity sufficient to account for the type of activity which it represents. In addition to this, however, we found a surprisingly powerful action of the choline type. When we extracted the fresh organ with precautions learned by experience, this activity was sometimes of such intensity that, if due to choline itself, it would have meant the presence in the extract of some 20 to 30 g. of that base per kilogramme of spleen substance. Such a proportion was incredible, and a clue to the

meaning of this activity was soon given, by the fact that it disappeared if the original extract, or its partially purified constituents, were exposed to an alkaline reaction. Chance had apparently presented us with an intensely active and unstable choline ester, naturally present in an animal organ, and in such proportion that the attempt to isolate it was a reasonable enterprise. The evidence, afforded by this instability to alkali, was reinforced and given very significant direction by the discovery that the extract lowered the arterial pressure, stimulated isolated intestinal muscle, and produced the abnormal, slow contraction of denervated voluntary muscle; and, further, that in each of these different actions it could be accurately matched against the same proportionate dose of acetyl-choline. The isolation and the chemical and physiological identification were completed by my colleague Dr. Dudley and myself only a few days ago, and we are able now for the first time to state that the substance is, indeed, acetyl-choline. The details of the evidence will be published shortly.

Some Physiological Implications.

We do not suppose that the finding of acetyl-choline in the spleens of certain animals has necessarily any significance as regards that organ itself, or that its presence suggests its action as a true hormone. The extraordinary instability of acetyl-choline in the blood makes such a function highly improbable. We regard the identification as important, chiefly for the reason that acetyl-choline, which first came to notice as an artificial substance, and has hitherto been known only as such, or as a product of plant metabolism, and as having a remarkable action on certain animal functions when artificially applied, is now known to be a natural constituent of the animal body. Where we have evidence, then, in the animal body of a substance resembling acetyl-choline in all its detectable characteristics, but in quantities or under conditions which give slender hope of its chemical isolation, this new knowledge seems to me to create a strong probability that we are dealing with acetyl-choline itself, and not with some unknown substance having similar properties. It seems to me, further, that we obtain a powerful reinforcement of this probability, if we consider its bearing on the relation to one another of a number of hitherto disconnected physiological phenomena. I will endeavour to arrange them in a logical sequence.

In the case of the inhibition of the heart by the vagus the liberation of acetyl-choline in relation to the heart muscle seems to fit the known facts, including the annulment of both vagus and acetyl-choline actions by atropine. It would seem difficult, then, to suppose that the vagus produces its stimulation of intestinal movements by an entirely different process; but here we meet the first discrepancy, in the fact that atropine very readily annuls the effect on intestinal movements of acetyl-choline applied through the surrounding medium, but not the otherwise similar effect of vagus stimulation. This is a type of discrepancy which we shall meet several times. It must be frankly recognised, but I doubt whether it should be accorded the decisive significance, which some have been disposed to attribute to it. We do not know how atropine prevents the action of acetyl-choline applied to the cells from the surrounding fluid; and it may be that, in some cases, it is peripherally liberated by nerve-impulses in such an intimate relation to the reactive structures that atropine is relatively ineffective in hindering its action.

Proceeding a step further, if we accept the mediating action of acetyl-choline in vagus effects, it is difficult to imagine that other parasympathetic actions, such as the vaso-dilator effects of the *chorda tympani*, are produced by a different mechanism. We have here again the same discrepancy with regard to the action of atropine; but, on the other hand, the supposition that this vaso-dilator action is due to peripheral liberation of acetyl-choline brings an entirely different, and otherwise unrelated, set of phenomena into the picture. As long ago as 1863 Vulpian and Philippeaux [26] described a curious behaviour of the tongue muscle, when deprived, by section and degeneration of the hypoglossal nerve, of its normal motor nerve-supply. Peripheral stimulation of the chorda-lingual nerve, or of the *chorda tympani* alone, now caused a curious slow contraction of the voluntary muscle, lifting and rolling the tongue; whereas in the normal tongue such stimulation causes nothing but vaso-dilatation. Now we have already noted that, under the same conditions, the tongue muscle shows a new, abnormal sensitiveness to a group of substances having a "nicotine" action, among which acetyl-choline is conspicuous. On injection of acetyl-choline into the circulation the denervated tongue muscle responds with the same kind of long, slow contraction as it exhibits when the chorda-lingual nerve is stimulated. In the normal tongue, therefore, chorda-lingual stimulation and acetyl-choline injection produce only vaso-dilatation; in the denervated tongue both produce an abnormal tonic contraction of the voluntary muscle. The suggestion is inevitable, that, when the *chorda tympani* is stimulated, a substance is released at the periphery, normally concerned in the tongue only with parasympathetic vaso-dilatation, but capable of exciting the abnormal, slow contraction in muscle-fibres deprived of their motor nerve-supply. We now know one substance in the body, and only one, which could produce both these effects, and it is acetyl-choline.

One further step brings me to the point of most importance for the general subject of these lectures. In 1894 Sherrington observed that degeneration of the motor nerve-fibres to the muscles of the leg caused a new type of reaction. These muscles now responded by a slow, weak tonus-wave to stimulation of the sensory fibres left in the sciatic nerve. Here, again, we have seen that a new and abnormal sensitiveness of the muscle-fibres to acetyl-choline appears, at the same time as this abnormal reaction to peripheral stimulation of the sensory nerve-fibres. And again, in the sensory fibres, we are dealing with nerve-fibres the peripheral stimulation of which normally causes no discoverable effect but vasodilatation, closely similar in its character and distribution to that produced by acetyl-choline, and differing only in that, like that caused by the *chorda tympani*, it is insensitive to the paralysing effect of atropine. Again the suggestion is inevitable, that the vasodilatation produced by antidromic stimulation of sensory fibres, or by the axon-reflex through their terminal branchings, involves the liberation, in relation to the affected arterioles, of a substance causing normal arterioles to dilate, and exciting voluntary muscle, deprived of its motor nerve-fibres, to an abnormal, slow form of contraction. The only substance known to occur in the body, and producing both these effects, is acetyl-choline; and it is unique among all known substances, from any source, in its power of producing both.

There is yet another point of correspondence which is worthy of notice. Frank, Nothmann and Hirsch-Kauffmann,[17] who first described the action of acetyl-choline on the denervated dog's tongue, showed that its effect, and the similar effect of stimulating the chorda-lingual nerve, were both suppressed during the circulation of a moderate dose of adrenaline in the blood. This parallel annulment, of acetyl-choline effects on denervated muscle and those of vasodilator nerve stimulation, appears not to hold good for the cat's tongue; but according to Hinsey and Gasser[27] it does so for the "Sherrington phenomenon" in the cat's hind limb. This action of adrenaline is incompletely understood; Gasser and I concluded that in some way it prevented the access of acetyl-choline to the reactive structures in the denervated muscle. If this is a true conception, the similar interference of adrenaline with the effects of stimulating the nerves acquires a very direct significance.

The probability, created by these items of evidence, of the intervention in arterio-dilator effects of a peripherally liberated substance, which also stimulates denervated voluntary muscle, has not escaped previous

recognition. Bremer and Rylant[28] hint at it, Hinsey and Gasser[27] suggest it as a definite possibility. With the knowledge now available, I am emboldened to give it precision, and to indicate acetyl-choline as the agent concerned. If this view is adopted, the local vascular reaction to stimulus or injury of the tissue, Lewis's "triple response," becomes, indeed, an interesting complex of pharmacodynamic effects. We have first the liberation of histamine from the immediately affected cells, directly causing vasodilatation of the minute vessels with which it comes into contact, and acting as a persistent stimulus to the sensory endings of the terminal axon-branching. So far we follow Lewis and the "H-substance." We must then further imagine that the nerve-impulses thus engendered, passing through the bifurcation to the ending of the collateral on the arteriole, there liberate, as the effective dilator, acetyl-choline. Such a conception may seem complicated; but in reality it makes for simplicity, in that it brings into coherent relationship a number of otherwise disconnected facts. The conception is, further, in harmony with the general tendency of neurological speculation to picture the intervention of a chemical agent, wherever an impulse conducted along a nerve-fibre becomes translated into excitation or inhibition of a cell, even at the synapses in the central nervous grey matter (cf. Sherrington[29]).

Other Possible Cases of Chemical Transmission.

For the autonomic system in general, this idea, that the arrival of nerve impulses at the peripheral endings may act on the effector cells indirectly, through liberation of a chemical agent, is not of recent origin. As long ago as 1904[30] Elliott suggested that the true sympathetic nerves might so act, by the liberation of adrenaline at their synaptic unions with plain muscle and gland cells. Such a conception is now supported, not only by analogy with parasympathetic effects, but by the direct observation, made by Loewi (loc. cit.) and confirmed by others, that the sympathetic, accelerator effect on the isolated frog's heart involves the liberation of an accelerator substance. We have no evidence, however, as to the chemical nature of this agent; and, likely as it may seem on general grounds, I think it would be rash to assume as yet, from the action alone, that adrenaline is the substance in question. The case made for acetyl-choline, as the transmitter of parasympathetic and sensory collateral vasodilator effects, is based partly on the chemical behaviour of the vagus substance, partly on the reproduction by the nerves of another aspect of its action, seen only on abnormal tissues, and quite unconnected with parasympathetic effects. There is no other such side to the action of adrenaline; and it remains a possibility that sympathetic nerves liberate peripherally another sympathomimetic agent, adrenaline being a special substance with properties fitting it peculiarly for the distribution of this type of action through the circulation. That other sympathomimetic substances may occur in the tissues is suggested by the effects of certain extracts recently described by Collip; but we have yet no knowledge of the chemical nature of the substance or substances concerned, nor any ground for connecting their existence with any known bodily function. Whatever be the nature of this suggested chemical intervener between sympathetic impulses and effector cells, it can serve only as the transmitter of centrally originated impulses. We have no evidence of any mechanism for the localised, peripheral release of adrenaline or of any substance acting like it; nor do we know of any normally functional peripheral-reflex mechanism concerned with sympathetic axons, or with nerves releasing any sympathomimetic agent. Broadly the contrast, indicated in an earlier lecture, appears to hold good; vasomotor effects, whether produced by nervous impulses or by hormones, are centrally originated and widely distributed, and are concerned with the upholding and mass-variation of vascular tone; vasodilator effects are largely, though not entirely, local reactions, chemically originated, and concerned with the finer adjustment of blood-supply to local requirements.

Some General Considerations.

I have endeavoured in these lectures to put before you the evidence concerning the part played in the control of the circulation by four chemical agents in particular. I have restricted my attention to these, not only because I have, in different degrees, been personally concerned in the investigation of each, but because they seem to me to be the only ones of which our knowledge is yet sufficiently definite to warrant even provisional conclusions with regard to their normal functional significance. A large amount of evidence exists on the effects of extracts from various organs of the body, artificially injected, or applied to isolated preparations of cardiac or involuntary muscle. A great many of these data can, as yet, be regarded only as observations put on record for future interpretation. To take only one example, there is a large amount of evidence, among the prominent contributors to which Demoor[31] in Belgium and Haberlandt[32] in Germany may be mentioned, on the effect of extracts from the right auricle, or from the sino-auricular junction, on isolated heart muscle. The suggestion has been made that some of the stimulating or restorative effects of such extracts on the rhythm of this muscle may be due to the presence of histamine; it has also been denied. It appears to me that we have not yet sufficient evidence as to the chemical nature of the substances concerned, as to their normal liberation, or as to the manner in which their effects could be produced under natural conditions, to justify the assumption that such an extract contains a "heart hormone" or an "automatin." We really need a system of criteria or postulates, comparable to Koch's celebrated postulates dealing with the ætiological significance of a micro-organism—conditions which must be fulfilled before physiological significance is attributed to the effects produced by artificial application of an artificial organ extract. There can be no hope, however, that any such criteria as could at present be suggested would be more generally applicable, or less liable to exception, than Koch's postulates have proved to be in their own sphere of application.

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THE MECHANISM OF FILARIAL PERIODICITY.

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THE difficult problem of filarial periodicity has puzzled and fascinated many since Sir Patrick Manson discovered its existence 50 years ago in *Filaria bancrofti*. Any attempted explanation must not merely account for the fact that the embryos of some filariæ are present in the cutaneous blood at all hours, of others by day only, and of yet others by night only, but must explain the established observation that the microfilariæ of *F. bancrofti* are in some parts of the world almost completely absent from skin blood by day, but in others can be found there throughout the 24 hours. A reasonable explanation of the periodicity, or of the lack of it, in *F. bancrofti* is obviously the key to the whole matter, and to the consideration of that anomaly this note is essentially directed; unless otherwise stated it is to this species that reference is made.

Periodicity in *F. bancrofti* is evidently produced in one of two ways. Either there exists in the circulation a fixed or almost fixed filarial population which shelters in some internal part of the body during the day and reaches the cutaneous capillaries at night only, or parturition is so timed that microfilariæ enter the blood stream at night only. The latter alternative implies: first, simultaneous cyclical parturition, using the term with the same loose regard to exactness as occurs in the reference to simultaneous cyclical sporulation in the tertian or quartan malaria parasites; and, secondly, daily death of the cyclical brood. The former conclusion was that reached by Manson, and it has held the day almost completely ever since. It seems well to reconsider it now in the light of the further knowledge which has been added to the subject particularly by the four expeditions sent out by the London School of Tropical Medicine which Manson founded, and by Prof. F. Fülleborn[1] whose recent survey of filariasis constitutes so remarkable an aid to all who would study this infection that without it the writing of this note might well have continued to be indefinitely postponed.

If microfilariæ merely retire to deeper parts during the day, what are those parts? Manson's[2] answer lay in their distribution in the organs after death in a classical case which during life had exhibited a very exact nocturnal periodicity, as proved by numerous examinations made during the previous nine months. During this period microfilariæ had been shown to disappear from the cutaneous circulation about 8 A.M. The man killed himself with prussic acid about 8.30 one morning in 1897. From the subsequent findings Manson concluded that "Filaria nocturna during its temporary absence from the circulation is present in the larger blood-vessels, particularly the arteries . . . but that the majority are lodged in the blood-vessels of the lungs." Now true filarial periodicity is marked by a swarm of embryos in the skin blood at night with their complete or almost complete disappearance from it by day; the difference is usually striking. If these microfilariæ shelter predominantly in the lungs by day, post-mortem examination should find them there in swarms when death occurs by day and in negligible quantities when it occurs at night. The difference should be a striking one if such examination can, as has been held, form a basis for conclusions. There is, at least, one such comparison reported. In British Guiana, where *F. bancrofti* shows nocturnal periodicity, Anderson[3] examined two cases who died of the acute septicæmia locally known as abdominal filariasis, one having died by day and one by night. Taking into consideration counts of microfilariæ found in those organs only which were examined in both cases, the percentage of the total which was found in the lungs was 23 for the day-time death and 10 for the night-time one. This difference in no way represents the loss of microfilariæ from the skin which occurs by day; it does not support a pulmonary habitat; and, quite reasonably, might be considered as fortuitous. Regarding the suggestion that microfilariæ retire by day to the large vessels, it is essential to remember that these creatures have no means of fixation. That they should be able to maintain their situation in the aorta or carotid artery seems as impossible as that a man should keep his position swimming against the current half way down the Niagara Falls. Moreover, Fülleborn has recovered enormous numbers of microfilariæ in the heart's blood after death, when puncture during life had recovered no more there than were present at the same time in skin blood. The post-mortem finding in Manson's case is not then evidence of microfilarial habitat during life, so far as the arteries are concerned.

Fixation in the Capillaries.

Fixation in the capillaries presents no such physical impossibility, and it has been held that during the period in which they are absent from the skin, microfilariæ retain their position in deep capillaries such as those of the lungs, either actively or passively. A retention, passive so far as the embryos are concerned, implies that during the period of their disappearance from skin blood the lung capillaries contract and retain the microfilariæ within them. But this means that such contraction maintains itself only at night when there is infection with *F. loa* in Africa, must be absent day and night when there is infection with *F. perstans* in Africa or with *F. bancrofti* in Fiji, and must be present only by day when there is infection with *F. bancrofti* in India or British Guiana. The corresponding constrictor effect of mixed infections on these vessels is too harassing to think out. Accordingly Fülleborn holds that *Mf. bancrofti*, in countries where it shows periodicity, takes up by day a slightly bent attitude and by this means holds itself for hours in deep capillaries and precapillaries, much as does a rock-climber in a cleft on the face of a cliff. Now such a "ratchet-action" posture is a commonplace in hookworm larvæ, but seems never to have been noted in microfilariæ. It is surely inconceivable that a posture adopted by the embryo for hours at a time in blood within the vessels should be absolutely abandoned in drawn blood. Moreover, Manson[4] aspirated by day the spleens of two filarious patients with nocturnal periodicity and drew off no microfilariæ. A small quantity of hæmoptysis blood passed by day was equally negative. W. W. Myers,[5] too, had negative results from both liver and spleen punctures in like conditions. During life, then, no secret day-time haunt of living microfilariæ has ever been detected. Furthermore, if one may so put the matter, what biological necessity could possibly induce the embryo to take up for many hours of the 24 an attitude which, on the supposition that it is long-lived, is entirely purposeless? That is the actual position. If embryos are long-lived and have already reached the blood stream they merely need to circulate there passively day and night till they die or are picked up by a mosquito. That microfilariæ must be passing through the skin capillaries during the hours when the insect vector feeds is essential for the preservation of the worm species; but that long-lived embryos should take the trouble actively to keep out of the skin at hours when the vector is unlikely to feed can advantage them in no possible way unless the mere fact of circulating damages them. That suggestion cannot be accepted for, assuming that *Mf. bancrofti* survives more than 24 hours, then in Fiji it enjoys no such respite from battering, and yet P. H. Bahr[6] holds that every embryo which reaches the Fiji vector, *Aedes variegatus* var *pseudoscutellaris*, probably proceeds to develop; Manson had shown that the periodic and presumably protected form in China enjoys no such vitality in culex. The conclusion, then, seems inevitable that the temporary withdrawal of the microfilaria by its

own activity from the skin during the day would be a biologically purposeless waste of energy subserving in no way the survival of the species and constituting a happening presumably impossible under natural selection. Yet it was just the presence of periodicity which led Manson rightly to implicate the mosquito as vector. The connexion must be in another direction. Again, microfilariæ are notoriously active creatures, and on the analogy, admittedly incomplete, of hookworm larvæ which are markedly altered in appearance after prolonged exertion, it is unexpected to find a complete absence from microfilariæ of any reported change in this direction, provided always that they live for long periods.

If periodic microfilariæ do not normally inhabit the large vessels during the day, how is their presence there after death explicable? If, as is by analogy reasonable, the female filaria in a dying host is apt to empty her uteri of microfilariæ, these, passing through the thoracic or left lymphatic duct, must later be found exactly where they have so frequently been reported after death, but as has been noted, not during life—in the lungs and large vessels.

Cyclical Parturition.

Passing to the possibility that periodicity in *F. bancrofti*, when it occurs, is an expression of parturition so timed that microfilariæ enter the blood stream at night only, it is clear that the necessary corollary is their complete destruction every day. The likelihood of periodicity by parturition was examined by Manson[4] in answer to certain observations by Myers.[5] Manson obtained and tabulated from the same man for six consecutive days and nights three-hourly counts of microfilariæ in smears of blood measuring 1½ by 1 in. and in the deposit from one ounce of chyluric urine. He then added together the counts from smears made at the same hour and wrote of the result: "If these figures are added together the results of this examination become more apparent. It seems to me that they indicate that filarial embryos are nearly always passing into the lymph stream. . . . Therefore filarial periodicity is independent of the act of parturition which is more or less a continuous process." The actual figures were as follows:—

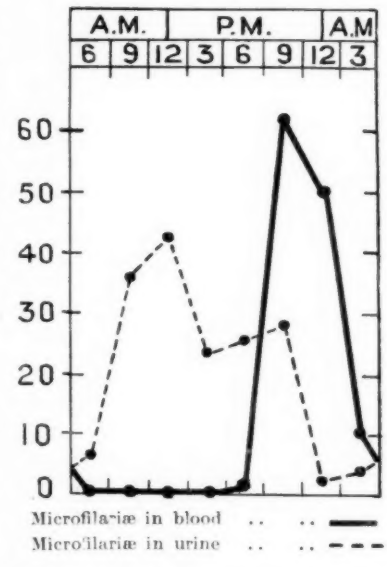
			Mid-day.				Mid-night.	
Hour	6	9		3	6	9		3
Microfilariæ in—								
Blood	0	0	0	0	1	62	50	10
Urine ..	7	36	43	24	26	28	3	4

If this Table be plotted out it produces the accompanying graph which does not indicate a more or less even microfilarial content of the urine and so of the lymph. There did, in fact, exist urinary periodicity, marked though not complete, and timed differently to that of the blood. This is just what would be expected since, as P. A. Buxton[7] writes, "the larvæ which are counted in the blood come from a parent which is causing no physical signs," they take a direct and rapid route down the lymph stream into the blood stream. The larvæ counted in this case in the urine came from a female lying behind a grave lymphatic blockage. The lymph bearing them must have taken a devious, slow, and erratic course to the ruptured lymphatic vessel in the bladder, so that the curve showing microfilarial discharge must be a flattened one with its rise considerably delayed—such a one, indeed, as the chart shows to have been present in this case.

Direct evidence concerning cyclical parturition is scanty; faced with the adverse opinion of weighty authority few, perhaps, have cared or troubled to collect apposite evidence. Yet scattered observations support it. Bahr[6] in Fiji reported upon six full-grown female worms. Two of these were without embryos but with eggs, and measured 50 mm. and 67 mm. long, the latter, indeed, being the largest individual recovered, and clearly mature. Presumably, then, they had emptied their uteri of microfilariæ, and were waiting for their next cyclical parturition.*

* The suggestion is that in these non-periodic filariæ parturition cycles of different females fall to be simultaneous.

Regarding their life span, he noted seven instances in which microfilariæ disappeared permanently from the blood while this was being regularly examined. In three cases this complete disappearance occurred within 24 hours of the onset of a febrile inflammatory reaction. Now Manson had noted, and O'Connor[8] has confirmed the observation, that mere fever does not cause microfilariæ to disappear from the circulation Bahr's observation implies, then, that the stream o newly born microfilariæ was abruptly cut off by the death or the complete inflammatory isolation of their mothers, and that those embryos already in the blood stream died within 24 hours. That the life span of microfilariæ in the body does not exceed a few hours is also suggested by another observation by Bahr. He found that in citrated blood they never survived for more than 12 hours at blood temperature, while his controls in the same citrated blood lived for three days at room temperature. Their survival at bench temperature for days is, of course, a commonplace, and is perhaps a necessity for survival in the mosquito.



Regarding the daily complete destruction of microfilariæ demanded by a simultaneous cyclical parturition which produces periodicity, microfilariæ have been injected into the blood of apes and have forthwith disappeared. Fülleborn[1] has, however, reported that *Mf. repens* injected into the dog has survived for two and three quarter years, and in one case doubled in size. These are biological unlikelihoods; and in connexion with larval longevity Myers[9] calculated, on the basis of Manson's investigations on *Filaria corvi-torquati*, that each female *F. bancrofti* poured 2,000,000 embryos into the blood daily. If these could survive for two years, the attempt to envisage traffic conditions in the blood and lymphatic vessels of a man parasitised by even a single female filaria for that period suggest that the term "unlikelihood" used above is a moderate one.

If microfilariæ are so short-lived, how are they disposed of? Evidence lies in two directions. Myers's[5] experiments, carried out with striking care and thoroughness, indicated that death and solution of microfilariæ (which showed periodicity and were evidently kept at the bench temperature of his China station) actually occurred in serum, and was much more rapid in morning than in evening blood. Manson[4] failed to confirm this, and the matter has evidently been dismissed as settled; but a positive finding from experiments as carefully executed as were those of Myers cannot be held cancelled by lack of confirmation from others carried through in unstated conditions. Moreover, this question of solution of microfilariæ can no longer be dismissed summarily as an irrelevance. Fleming's[10] showing—that 5000 million *Micrococcus lysodeikticus* are dissolved in a few moments by a tiny tear, and that the lysozyme which is the active principle concerned, and which is present in white of egg, still has lytic action

when this last is diluted to 1 in 60,000,000—compels reconsideration of this matter.

Actual destruction of microfilariæ in the body itself has been observed by E. Rodenwaldt[11] and by Anderson.[3] The former implicated the renal medulla where he found disintegrating embryos so plentiful that Fülleborn refers to these organs as constituting a veritable microfilarial cemetery—as the place where dead and dying microfilariæ are eliminated from the blood. Anderson found in the liver and spleen, and apparently in the lymph glands, dead microfilariæ without striation and in process of dissolution. These records are few enough, yet the doctrine of periodicity by visceral filtration is so venerable and carries such a weight of authority that regular investigation into possible massive destruction of embryos has never been conducted, so that the fact that such a condition has not been regularly reported is no necessary evidence that it is not regularly taking place. The matter at least merits deeper study.

Biological Support.

But the consideration which appeals most strongly to the writer as supporting simultaneous cyclical parturition as the cause of periodicity is biological. Speaking generally, two typical mosquitoes serve *F. bancrofti* as intermediate host, *Aëdes variegatus* var *pseudoscutellaris* in Oceania where it bites mainly, but as O'Connor showed, not exclusively by day, and where the microfilaria is non-periodic, and the night feeder *Culex fatigans* elsewhere where the microfilaria is periodic and nocturnal. Both these insects Bahr fed on the same filariated patient in Fiji where microfilariæ are non-periodic. The work was a model of control. In *C. fatigans* the infection in the majority of insects died out altogether; in no instance were more than two developing filariæ found in the thorax of one mosquito after the seventh day. On *A. pseudoscutellaris*, on the contrary, it was deemed possible, as already mentioned, that all microfilariæ which had been imbibed had proceeded to continuous development; at all events as many as 38 were found in the thorax of one mosquito on the sixteenth day, and feeds from strongly infected blood caused so heavy an infection that the mosquitoes died. As a secondary host *A. pseudoscutellaris* is then many times more susceptible than *C. fatigans*.

The influence of this susceptibility on the worm species will be much as follows. Infected aëdes will die in thousands from filarial infection, but this is biologically immaterial to the filaria, since the number of vectors which survive is so great and the output of microfilariæ so prodigal that the species will be maintained with ease by those other mosquitoes who happen to become lightly infected. Even with a heavy human infection, mosquito infection may be light, either because the insect happens on a moment when the circulating blood contains few microfilariæ (Bahr has shown that the microfilarial content of the blood may vary in Oceania from minute to minute), or because it secures a small meal only. Should such filariæ be carried by the migration of their human host out of the relatively restricted area of this optimum intermediate host into that of *C. fatigans*, where an increase of the microfilarial content of the cutaneous blood at night is essential, then, if the species is to maintain itself by means of this inefficient "nurse" when the human host is lightly infected, no juggling by retention of microfilariæ in deep organs can add to their number in the skin and perpetuate the worm species in these new and difficult conditions. Just the reverse. But if the female worms, without altering the number of short-lived microfilariæ produced daily, can learn under some stimulus at present unknown so to regulate their already varying rate of parturition as to concentrate cyclically in the blood, the great bulk of these embryos during the few hours when *C. fatigans* bites, the worm species will survive even with this inefficient intermediate host. While this sequence assumes that Oceania is the original home of *F. bancrofti*, there seems, if it is worked out mentally in detail, no insuperable biological reason against the process having been the reverse. Yet an optimum insect host and an unspecialised type of parturition seem to be primitive characters. That the contrary has been commonly assumed is, perhaps, due partly to the prior discovery of the periodic form, and partly to the knowledge that the trend of the "Archaic Civilisation," as W. J. Perry[12] calls it, emanating probably from Egypt, travelled thence eastwards by India right across the Pacific. Yet these pioneers went out for commerce and brought back west and north gold and pearl shell. And just as later the European civilisation searching America for gold brought back the potato and syphilis, so is there good reason to believe did the Archaic Civilisation not only carry the taro plant from India into the Pacific and carry it back to Egypt, whence it has spread across Africa, but also, it is here suggested, transport *F. bancrofti* westwards. The direction of transport is, however, for the purpose of this note, relatively unimportant. The essential point is the insistence that the trend of evidence supports, as the mechanism producing periodicity in *F. bancrofti*, simultaneous cyclical parturition and daily massive destruction of microfilariæ.

Conclusions.

The conclusions reached regarding the mechanism of periodicity are these. If the embryos of *F. bancrofti*, when absent from the skin blood, harbour elsewhere, it is physically unthinkable that they should do so in the overwhelming current of the large blood-vessels; they accumulate in these in numbers from the lymph trunks at or after death only. Nor are they being held back from skin blood by contraction of visceral capillaries, since these can hardly close on one species and open for another circulating in the same blood at the same time. If it were their posture which maintained microfilariæ for many hours daily in deep capillaries, posturing would not be completely discarded in drawn blood. Living microfilariæ have never been found congregated by day in any deep capillaries in numbers corresponding in any way to those demanded by this hypothesis of the mechanism of periodicity; no secret retreat of theirs has been discovered. If they were long-lived, old should be distinguishable from young larvæ by visible changes induced by their activity. Periodicity, then, cannot reasonably be explained as being due to a changed distribution within the blood-vessels of long-lived microfilariæ. Moreover, such a condition holds no biological advantage for the species.

The known facts have a cumulative weight in favour of the hypothesis that microfilariæ within the body perish rapidly, at least daily, and that periodicity is the result of simultaneous cyclical parturition. It is by this device alone that, except in optimum circumstances, the species is enabled to survive. Periodicity, then, is not a mere adaptation to the feeding habits of a particular intermediate host. It is an adjustment which produces that mean between failure to infect an insect and liability to kill it by hyperinfection which reasonably subserves the survival of the parasitic species. It is suggested that contentment with present beliefs on present foundations is no longer possible, and that the whole matter needs reinvestigation with an open mind.

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PRIMARY GENERALISED HYPERTROPHY OF THE GUMS.

ILLUSTRATED BY A CASE.

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THE entity of most rare conditions is difficult to establish and the case which I describe is no exception. Many authors, among them Grieg, Heath, Sleep, Parkes Weber, and Ironside, have pointed out the rarity of this condition. Heath says that the first case recorded in England was by S. J. A. Salter in 1859, occurring in a little girl aged 8 at St. George's Hospital under the care of Pollock.

Précis of Current Views.

There is some confusion in the literature about the existence of this condition as a separate entity from the rare unilateral hypertrophy of the gums which may be general or localised. The credit for giving us a clear picture is due to Grieg, who thinks that this form of hypertrophy does not constitute a disease, but an affection sui generis, a pure overgrowth of the gums, which is congenital, general, and bilateral, and only gives rise to discomfort after the eruption of the teeth, temporary and permanent alike. Many authors agree that the condition is congenital.

(*a*) Salter thinks it is congenital; although it occurs in children, it has never been known to occur at birth.

(*b*) Hutchison points out that the hypertrophy of the gums, in his case, preceded the appearance of the teeth which had never been able to force themselves beyond the gum surfaces; they were somewhat carious and would probably come out. If the condition were the result of sepsis of the gums or of pyorrhœa, one would expect it to be commoner. He compares it with macroglossia and—if the term were permissible—one could call it "gigantism of the gums."

(*c*) Sleep gives excellent reasons for assuming a congenital origin. He does not consider the lesions to be contingent on any exciting cause, but that the potentiality was contained ab initio in the germinal vesicle itself. As he says, "constitutional perversion is a developing force that precedes and accompanies the advent of the teeth germs from their genesis to their maturity." The teeth in his cases were normal in size and shape; there was no suggestion of any pathological process or excitement in the fœtal or infant life which might have induced hypertrophy of the formative epithelium constituting the enamel organ, or the submucous tissue of the papillæ forming the dentine. He therefore correctly infers that the aberrant process underlying the disease may precede the advent of the dental organs and grow with it and that they should not be suspected as the possible causes of the disease, either by or through their mere presence.

(*d*) Allbutt and Rolleston, discussing the causes of hypertrophy of the gums, mention that generalised hypertrophy may be due to widespread dental disease, especially when the organisms and pus form in pouches between the teeth and the gums, as in pyorrhœa. They are careful, however, to notice that there is a deep-seated general hypertrophy which is congenital, although it may only be noticed at the first dentition. They say that it is necessary to shave off not only the gums but also the portions of the dental alveolus from which it grows. I have no doubt that these authors have in mind the conditions which we are discussing.

(*e*) Humphry, in his monograph on a condition which was unilateral only and associated with other abnormalities such as hyper-development of the left side of the face, tongue, and palate, thought the condition was a simple but spreading hypertrophy of the gum tissue, which was either congenital or began in very early life, perhaps at the cutting of the first teeth. He mentions that it commonly involves the entire gums of both jaws on both the buccal and the palatal side.

On considering the various views, I agree with Grieg that the condition is a congenital one which does not manifest itself until the eruption of teeth.

Association of Hypertrophy with Mental Deficiency.

In discussing hypertrophy of the gums many authors have, I think, copied each other slavishly, and reiterated the fact that hypertrophy of the gums is associated with mental deficiency. Hopson, for example, in his discussion of the ætiology of this condition, says "there is no defective mental condition in this case, as is so often associated with these cases of hypertrophy." Again, Canton showed a case of hypertrophy in a half-witted and strumous subject; he regards the patient's condition as the cause of the hypertrophy. It is true that in some of the cases reported mental deficiency was present, but the condition is not always associated with weakness of intellect. Sleep says that the real cause seems to lie deeper than mere constitutional debility, infection, or even intermarriage, though it is generally understood that the last-named is capable of awakening latent proclivities to disease and intensifying vicious tendencies, physical and psychical. Grieg, discussing the various views, is sceptical about Erichsen's opinion on mental deficiency and hypertrophy of the gums, and does not think his experience among the mentally deficient was large enough to enable him to draw correct conclusions. Grieg had 25 years' experience among the feeble-minded and he infers that no such hypertrophic condition can be noted as peculiarly associated with mental defect. Humphry quotes ten cases, of whom three—namely, the cases of Gross, Murray, and Waterman—possessed feeble intellect. He remarks that hypertrophy of the gums is often associated with other abnormalities, but he was discussing his remarkable case in which the hypertrophy was left-sided only and associated with hyper-development on the left side of the soft palate, tonsil, alæ nasæ, eyelids, pinna of the ear, eyebrows, papillæ of the left side of the tongue and of the face generally. He also quotes ten cases of general hypertrophy of the gums, among which three were of feeble intellect, one had stunted growth, an ill-shaped head, and a protruberant abdomen, two were epileptic, two had abnormal growths of the hair on the body, and one was deaf. Among the cases reported many such defects have been found associated with hypertrophy of the gums, but many of these do not come under the exact category of the case I describe. In the remarkable series of cases described by Murray in 1873, several children, members of one family who suffered from molluscum contagiosum, also had hypertrophy of the gums. I think the condition of the gums was primarily due to this molluscous fibromatous disease, secondary inflammatory changes causing the hypertrophy of the gums. Again, Erichsen's case was one of the same series of children, and the enlargement was part of a generalised disease, neuro-fibromatosis.

FIG. 1.

Photograph of the patient showing hypertrophied gums and dense growth of eyebrows.

Association with Abnormalities of the Hair.

One other abnormality which I think is associated with this hypertrophy has not been sufficiently emphasised. This is overgrowth and irregularity in the growth and distribution of the hair. As the teeth and hair are dermal appendages hypertrophy of the gums may well be associated with excessive hairiness and fibroid enlargement of the skin.

1. Hopson mentions the celebrated case of one Julia Pastrana, who was a member of a family in whom the gums were much hypertrophied and the hair on the whole of the body was very largely in excess.

2. Humphry noticed that the hair on the head was thick and coarse and the vibrissæ in the nostrils were exceptionally long. The hair on the eyebrows of the left side was coarse and abundant, and spread over the median line.

3. Parreidt's case was an Indian girl, aged 7, who had hypertrophy of the gums and very well-developed growth of hair.

4. Waterman mentioned a woman of feeble intellect, who was exhibited by a Boston showman under the name of the "bear woman." She exhibited huge hypertrophied gums, and her body was covered with a remarkable hairy growth.

5. Pollock's case was noticed to have from birth an unusual quantity of hair on arms, legs, and head.

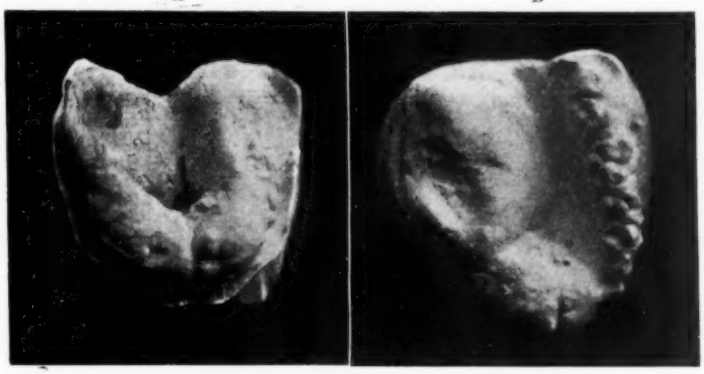
Description of Author's Case.

The patient, a french polisher, aged 20, came to me early in 1928 complaining chiefly of foul breath and bad taste in his mouth, and suffering from ulcerative stomatitis. He is the sixth member of a family of 11 children, all of whom are in good health, none of them suffering from bad teeth or showing signs of gingivitis. The parents are not consanguinous, are poor working-class people, and do not live under good sanitary conditions. The mother gives a history of three miscarriages, but has not suffered from any diseases except chronic rheumatoid arthritis. The father has fairly good health. The mother says: "The child never had teeth; at the age of 3 he was taken to the Metropolitan Hospital for that reason, and from there he was transferred to Great Ormond-street Hospital." Unfortunately, I have been unable to trace the history of the case at Great Ormond-street, the notes having been destroyed. According to his mother, his gums were there lanced top and bottom, to allow the teeth to come through, and she dates the hypertrophy of the gums from that date. The man asserts that he never had teeth from the age of 4 until the age of 19, and that he managed to chew on his enlarged gums. He never had rickets, or suffered from tonsils or adenoids or from enlarged cervical glands. He has had no other illness of any importance. He is a normally developed male, and is certainly not mentally deficient. He has no other physical defects. His hands and feet do not show any signs of enlargement, and the latter are in perfect proportion to his body.

The growth of hair on his body is rather remarkable. It is thick and black, and the distribution on his arms and legs is much denser than that of the average hairy male. The hair on his legs, however, is remarkable in that it is evenly distributed over the whole of the leg and does not stop at the pubic region but is continued on the buttocks and well above the sacral region and tapers up his spine. The hair is long and coarse in texture. On his face the hair is coarse and dense, and the eyebrows are extremely dense and continuous over the bridge of the nose. The texture of the skin of the face is rather coarse, and he has a sallow complexion and suffers from slight acne. His mother asserts that as a child the whole of his body was covered with very fine hair.

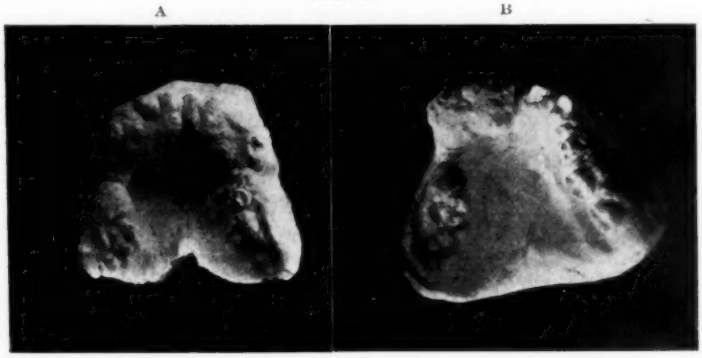
He has huge hypertrophied lips, upper and lower, his mouth being so prognathous that his lips cannot be comfortably strained over the hypertrophied gum masses, the mouth being always kept half open. Between the lips the hypertrophied masses of gum tissue look, as Heath described in one of his cases, "like the mouth of a hippopotamus or a rhinoceros on a small scale." (Fig. 1.)

FIG. 2.



Model of upper jaw (A) before operation, and (B) after operation. (It was impossible to take a complete impression owing to the size of the masses filling the mouth.)

FIG. 3.



Model of lower jaw (A) before operation, and (B) after operation.

Inside of the Mouth before Operation.

The tonsils were slightly enlarged and ragged. The uvula was enlarged and lengthened, and was approximated to the dorsum of the tongue. His tongue gave the impression of being long and thin, owing to its confined position between the hypertrophied masses of gum; but when protruded it was seen to be normal in size and shape.

The lips were pushed forward by the hypertrophied masses and the lower mass of gum tissue protruded, everting the upper larger mass. The gum tissue was of normal colour, but rather firm and coarse in texture.

Upper Jaw.—The hypertrophied mass (Fig. 2A) consisted of two ill-defined masses, one extending from the posterior right extremity of the jaw to the region of the left canine or premolar, where there was a dip in the tissue extending from the palata to the buccal side; the other from the second premolar to the left posterior extremity. This latter mass extended across the mid-line of the palate, meeting its fellow of the other side. The proximity of the two masses gave the impression of a cleft palate, the cleft posteriorly admitting only the thickness of a visiting-card, and anteriorly widening out into a diamond-shaped impression 1·5 cm. in its greatest diameter. The mass in the anterior region was 2·4 cm. thick bucco-palatally, the mass in the right posterior region 3 cm. thick, and that in the left posterior region 3·3 cm. The depth of the mass anteriorly from the under-surface of the gum to the reflection of the buccal mucous membrane was 2·5 cm.

The only teeth present were the upper right first and

second premolars and molars, and the left canine; only the tips of the cusps were showing, looking like an ivory island in a sea of pink flesh.

Lower Jaw.—This consisted of three ill-defined masses extending (1) from the right third molar to the right second premolar; (2) from the first right premolar to the left first premolar, where there was a dip extending to about the first molar; and (3) embracing the first to the third molars. (Fig. 3A.) The left mass in the anterior region was 1·9 cm. thick bucco-lingually, the left 2·2 cm. The right posterior

FIG. 4.

Skiagram of jaws.

mass was 1·9 cm. thick bucco-lingually, the left posterior mass 1·9 cm. bucco-lingually. The teeth present were the right second premolar, first right molar, left first molar and second molar. The teeth protruded to a depth of 1·3 mm. The buccal mucous membrane was raised in ridges, which partially covered the hypertrophied masses of gum tissue.

At St. Bartholomew's Hospital Mr. J. E. H. Roberts resected a portion of the gum on the right half of the upper and lower jaws.

Right Side of Mouth after Operation.

The teeth are displaced either inwards or outwards by the hypertrophied masses of gum tissue. The only one missing is the first incisor, which was extracted at operation. The incisors and canines are all inclined outwards; the premolars and molars face inwards—that is, lingually. Intervening masses of tissue cause undue and irregular spacing of the teeth. The top jaw (Fig. 2B) is similar to the bottom jaw (Fig. 3B) in appearance, and all the teeth are present.

It is important to have a dental report on the teeth, which now appear for the first time, as it may be suggested that the hypertrophy was due to infection, in which case there should be pathological changes in these teeth. One suggestion made to me by a dental surgeon was that minute sinuses might lead down to the teeth and through these channels infection might occur, the reaction causing lymphatic obstruction; hence the elephantine dimensions of the gums. Mr. Evelyn Sprawson, dental surgeon of the London Hospital, examined the teeth, and found that they were apparently normal and healthy. Skiagrams of the jaws (Fig. 4) showed that the whole of the permanent dentition was present except the incisor which was removed at operation, and the lower third molars, which were both congenitally absent.

Comparison of the models made before and after operation shows an increase in the hypertrophy in the unoperated side. This is due, I think, to the fact that the pressure of the operated side was removed. There is also a tendency for the hypertrophy to recur on the operated side. This fact has been noted by Grieg in his case, and also in a case quoted to me by Mr. Sprawson.

The Wassermann and sigma reactions of the blood were negative. A microscopical report on the section shows that the nature of the tissue is difficult to determine, but it apparently consists of chronic infective hypertrophied tissue with much fibrous tissue. I have examined microscopically a section lent to me by Mr. Sprawson, taken from a case of general hypertrophy of the gums. This section gives us the same microscopic picture as my case, and suggests that it is a form of defuse fibroma.

As the milk teeth never appeared, there should be evidence of their presence in the jaw bones. From the mother's history "that the child was brought to hospital because he had no teeth, and after lancing no teeth were found," we have good reason to suppose that our subject was a case of a congenital absence of milk teeth; moreover, there is no history of their having been lost. This in itself is a very rare condition. The radiogram of the present teeth gives no evidence of the milk teeth ever having existed. The fact that this man was abnormally hairy as a child, to my mind, strengthens the suggestion of absence of milk teeth. Many cases have been recorded of deficiency of teeth associated with abundance of hair. Colyer quotes the case of Andrian Jeftichfen, in whom the whole of the face, nose, forehead, cheeks, and ears were covered with long brown hair, which also extended partially down the back. His son, Fedor, at the age of 3, showed the same tendency to hairiness. The father had no teeth up to 17 years of age, and eventually only erupted four teeth in the mandible and one in the maxilla. The son, Fedor, at the age of 3 possessed only four incisors in the maxilla. The Burmese family, consisting of grandfather, mother, and son, are said to have been deficient in the number of their teeth, but there is no reliable record. Again, cases are known where entire absence of teeth was accompanied by marked deficiency of hair.

Deficiency of Teeth and Hair Correlated with the Pituitary Glands.

From the foregoing cases it is evident that there is a co-relation between the hair and the teeth; in one class there is a deficiency in both structures and in the other deficiency of teeth is associated with redundance of hair. From this one can, I think, deduce interrelationship with the pituitary gland, knowing as we do that the secretion of the anterior lobe is connected with the growth of the skeleton, skin, and soft tissues. Cushing, in his book on the pituitary gland, mentions hypertrichosis due to excessive secretion of the pituitary. In acromegaly there is osteal hypertrophy of the maxilla and overgrowth of the soft connective tissues and periosteal ends of the fingers and toes. Sleep also suggested a relationship between the endocrine system and the hypertrophy of the gums. McNeill Love has this year described a case of hypertrophy of the gums in a boy aged 18. His case is, I think, one of the rare types we are discussing. Love states that the hands and feet are undoubtedly large, and X ray showed enlargement of the sella turcica, yet Love suggests acromegaly as the cause of the deformity, stating, however, that there were no other signs of the disease present.

On embryological grounds there is evidence of the relation between the anterior part of the pituitary gland and the buccal cavity. The anterior lobe is developed as a tubular prolongation from the epiblast of the buccal cavity, the embryological stomodeum, but the growth of intervening tissue soon cuts off all connexion with the mouth.

I put this hypothesis forward as a tentative suggestion, but in our present state of knowledge of the endocrine system we must leave it to further research to elucidate clearly the exact function of the co-relationship of this intricate system.

I must express my thanks to Mr. C. H. Fox for his skill in constructing the models, and to Mr. Evelyn Sprawson for help and advice.

(*Bibliography at foot of opposite page.*)

A NOTE ON BLOOD TRANSFUSION.

WITH AN ACCOUNT OF A FATAL REACTION.

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In the case now reported death was the direct result of a blood transfusion. The patient was not gravely ill before the operation and the preliminary tests were made with care. I am therefore publishing an account of the case and a few notes from the literature of the subject. Transfusion is a relatively simple and safe operation and the great majority of deaths are due to errors in technique. Nevertheless, the operation is not absolutely devoid of risks even in careful hands.

Clinical History.

A woman, aged 29, had been anæmic since the birth of twins three years before. The confinement was normal and there was no excessive loss of blood. Since then she had suffered from shortness of breath, dizziness, and occasional swelling of the feet at night. Her symptoms were alleviated from time to time and then got bad again. There was no obvious cause for the anæmia. Her nutrition and general condition were good and there were no physical signs of disease apart from the anæmia.

She was treated for five months with iron and ammonium citrate, grs. 10 three times a day, and made no improvement. At the end of that time her blood count was: red cells, 3,800,000; Hb. 44 per cent.; colour-index, 0·58; white cells, 7300; neutrophiles, 60·0 per cent.; eosinophiles, 2·0 per cent.; basophiles, 0·5 per cent.; lymphocytes, 31·5 per cent.; monocytes, 6·0 per cent.; the platelets, the fragility of the red cells, and the van den Bergh reaction were normal. A fractional test-meal showed a complete achlorhydria. The urine was normal. It was decided to give a transfusion.

The patient was found to belong to group II., and a donor of the same group was obtained. Immediately before the transfusion, both the cells of the donor and recipient's serum and also the cells of the recipient and donor's serum were matched in the usual way (Panton and Marrack).[11] No agglutination occurred in either specimen. The donor had given blood four times before and "all his patients had done well." The citrate technique was employed and the transfusion went smoothly. The patient complained of headache but nothing unusual was noticed. A few hours later she was sick, and she vomited at intervals during the next 48 hours. She did not have a rigor but the temperature rose to 102·6°F., falling to normal in 48 hours. There was no jaundice. Pain in the back was not complained of till 48 hours after the transfusion. It then persisted till death but was never severe.

A rectal saline was given on the day after the transfusion. On the cessation of the sickness the patient took water, soda-water and orange juice fairly freely by mouth. No urine was passed till the sixth day, when six ounces of very acid urine were excreted. It contained three-fifth volume of albumin, the urea concentration was 0·69 per cent., the deposit contained a few hyaline casts, red cells, many leucocytes, and many epithelial cells. A casual observer would not have realised that the patient was in extremis. Her colour and appearance were good, her mentality clear, the pulse was 64, the blood pressure 120/80. Nevertheless, the blood-urea on this day was 333 mg. per cent. Potassium citrate was given by mouth in drachm doses six-hourly, but the patient began to be sick again and it was omitted.

On the seventh day intravenous injection of normal saline was begun, a pint being given three times daily. Eight ounces of acid urine were passed. On the eighth day grs. 30 of potassium citrate were also given intravenously. Five and a half ounces of acid urine were passed. On the ninth day the blood pressure was 150/90. The patient was drowsy. Two pints of saline and grs. 30 of potassium citrate were injected during the forenoon. In the early afternoon the patient had tetany, but this disappeared after the intramuscular injection of one grain of calcium chloride in 40 minims of water. In the evening of this day one pint of saline and grs. 5 of potassium citrate were injected. Soon afterwards the patient shivered and Chvostek's sign was positive. She was therefore given another injection of one grain of calcium chloride and no tetany developed. Later in the evening 1½ pints of saline were given intravenously. Eight and a half ounces of acid urine were passed on this day.

On the tenth day the blood-urea was 354 mg. per cent., the plasma bicarbonate 33·6 volumes. A pint and a half of saline was given intravenously. The condition of the patient seemed fair. There was no visible œdema, but as there were signs of bronchitis no more saline was injected. The urine, which had previously been strongly acid, was neutral. Eight ounces were passed. There was one-tenth volume albumin, and the deposit contained granular and hyaline casts, red cells, leucocytes, and epithelial cells.

In the early hours of the eleventh day the patient, who had been sleeping comfortably, suddenly sat up in bed and fell back dead.

Findings at Necropsy.

A post-mortem examination (No. 575, 1928) was made by Prof. H. M. Turnbull, and the following is a summary of the findings:—

Examination showed "bilateral pleural effusion (32 oz., right, 12 oz. left), ascites (18 oz.), great œdema of the lungs, œdema of the brain and other organs, and a general anasarca which was relatively slight in the subcutaneous tissue so that the skin did not pit; greatly enlarged kidneys (16½ oz., body 114 lb. 7 oz.) showing a few petechiæ, a swollen, pale, yellowish-grey cortex with obscured pattern, and a dark red-brown medulla; a few petechiæ in renal pelves; general anæmia; hæmatogenous marrow throughout the neck and upper three-quarters of the shaft of the femur and in a few patches beneath."

Microscopic Examination of Kidneys.—"Most of the discharging tubules are filled with fine granules, large lumps or, occasionally, homogeneous masses of an isotropic substance of the colour of brown sugar. In addition to this substance there are frequently many desquamated epithelial cells and neutrophile leucocytes; less frequently there are areas of hyaline albumin. Where the cytoplasm of desquamated epithelial cells can be identified it is finely granular and of the same colour as the granules and lumps. Similar casts occupy numerous collecting and junctional tubules; but in these tubules, especially in the junctional, the brown substance is frequently replaced by deeply eosinophile granules or small spheres, amongst which one or two red corpuscles are occasionally present. The convoluted tubules contain albumin in the form of a net or multiple spheres; the remaining tubules sometimes contain the same or hyaline albuminous casts, but they are more often empty. Within the convoluted tubules there are occasionally one or two red corpuscles. Beneath the capsule in one section there is a small group of tubules filled with red corpuscles. All the tubules are dilated, particularly the collecting. The capsule of Bowman is usually only slightly dilated, and contains pale albuminous spheres. The glomeruli are large, and show no sign of collapse. The basement membrane of their capillaries is swollen, whilst the capillary lumina are wide and rarely contain any red corpuscles. The anæmia of the glomeruli thus contrasts very conspicuously with an engorgement of intertubular capillaries and a great engorgement of the vasa recta. The epithelium of the first and second convoluted tubules shows a very severe albuminous degeneration. Karyokinetic

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figures in epithelial cells are frequent. The interstitial tissue throughout the medulla is greatly rarefied by œdema; the œdema in the cortex is patchy, but in these patches it is extreme. Round-cell infiltration is great round the vasa recta in the upper two-thirds of the medulla, and is considerable in the interlobar connective tissue, beneath the capsule, and in the adventitia of the vessels in the intermediate zone and in the cortex; it is occasionally present round discharging tubules filled with the characteristic casts. The infiltrating cells are chiefly plasma cells and large lymphocytes; small lymphocytes are less numerous; eosinophile leucocytes come next in frequency and in some foci predominate; histiocytes, neutrophile leucocytes, and large mononuclear leucocytes are relatively scanty. One or two myelocytes, myeloblasts, and normoblasts were found within capillaries on searching, but there is no myeloid reaction in the infiltration. There are interstitial hæmorrhages in the medulla round engorged vasa recta, in the interlobar connective tissue, and beneath the surface of a medullary pyramid. Fat, doubly refractive lipoid, and hyaline-droplet degeneration are absent."

The cause of death was suppression of urine following hæmoglobin infarction of the kidneys.

Discussion.

It is difficult to assess the inherent risk in blood transfusion. Most of the fatalities are due to faulty technique. Many of the patients are gravely ill and it may be doubtful whether death was due to the disease or the treatment. Much depends on the condition for which transfusion is given. In acute hæmorrhage severe reactions are rare. In the blood diseases reactions are more frequent and the blood group is sometimes so atypical that it is difficult to find a suitable donor. Severe reactions are so often encountered in the treatment of acute sepsis and acute leukæmia that transfusion is contra-indicated in these diseases. Bernheim,[3] in 1917, collected reports of 800 transfusions from 20 different surgeons. There were four deaths from hæmolysis. No tests had been made in three of these cases. In the fourth it was known that the donor's cells were agglutinated by the recipient's serum. There were six other deaths, four attributed to cardiac dilatation, and two to anaphylactic shock. Thus eight of the ten deaths were due to errors in technique. In the following Table I have summarised some of the more recent American figures, which show the results obtainable to-day. In over 4500 transfusions there were only five deaths, of which four—and possibly the fifth—were known to be due to errors in grouping.

Year.	Operator.	Preliminary tests.	Technique.	Total transfusions.	Deaths.
1919	Pemberton.[12]	Grouping.	Citrate.	1036	3
1923	Copher.[6]	Grouping plus cross-agg.	Citrate and direct	245	2
1925	Kordenat et al[9]	Cross agg.	,,	764	0
1928	Brines.[4]	Grouping.	Direct.	2500	0
	Total ..	..	..	..	4545	5

Agg. = agglutination.

Mr. P. L. Oliver has very kindly given me the figures for the Blood Transfusion Service of the British Red Cross Society, of which he is hon. secretary. This service has provided donors for 3430 transfusions. Five deaths have been reported. One of these was our own patient. Another was a man with advanced malignant disease who died of syncope during transfusion. In the third case the donor had been wrongly grouped, and in the fourth the patient had been wrongly grouped. In a fifth case the donor belonged to group IV, as was later confirmed by regrouping, but the patient, whose group is not given, died before the completion of the transfusion. It appears from these figures that the mortality of the operation of blood transfusion is of the order of 1–2 per 1000, and that the majority of the fatalities are due to inadequate compatibility tests. Members of group IV. can no longer be considered universal donors, as not a few deaths have followed the adoption of this simple "rule of four"; although the plasma of the donor is greatly diluted in the recipient, it is sometimes rich enough in agglutinating and hæmolytic principles to produce severe hæmolysis. There are few emergencies so urgent that it is not possible to do direct cross-agglutination tests with both donor's cells and recipient's serum and also donor's serum and recipient's cells. With this precaution severe reactions are exceedingly rare though they cannot be absolutely excluded.

In recent years, however, a number of fatal reactions have been described after transfusions although these preliminary tests had been carried out. These reactions are of two types, the hæmolytic and the anaphylactic. It is difficult to understand why hæmolysis should occur after a satisfactory cross-agglutination test. It is suggested (Doan)[8] that hæmolysin and agglutinin are not always present in proportionate amounts in the serum and a slight degree of hæmolysis may be overlooked in the test. Nevertheless, Percy,[13] in a series of 54 transfusions by the direct method, had three instances of severe hæmolysis and two of the patients died; in all three cases the blood of donor and recipient had been tested for hæmolysis before transfusion with negative results. A more probable explanation is that agglutinins are present in such low concentration that they are missed in the preliminary tests. Three instances of fatal hæmolytic reaction have been described in which preliminary grouping or cross-agglutination had been satisfactory, but on repeating the test after the development of the reaction the bloods were found to be incompatible (Baker and Dodds,[1] Copher,[6] Shera[15]). Schneider[14] has collected from the recent German literature an additional six cases in which fatal hæmolytic reactions occurred although there was no agglutination in the preliminary matching of donor and recipient. He is of the opinion that cross-agglutination is not a very sensitive test and that it is better to perform accurate grouping with high titre sera. There are great variations in the strength of agglutinin and agglutinogen in different bloods of the same group, and a blood may be allocated to the wrong group if the test sera are not fresh and active.

The effects of the transfusion of incompatible blood have been described by Pemberton.[12]

"The clinical picture of these reactions is typical. They occur early, after the introduction of 50 or 100 cubic centimetres of the blood; the patient first complains of tingling pains shooting over the body, a fulness in the head, an oppressive feeling about the precordium, and later, excruciating pain localised in the lumbar region. Slowly but perceptibly the face becomes suffused a dark red to a cyanotic hue; respirations become somewhat laboured, and the pulse-rate, at first slow, suddenly drops as many as 20 to 30 beats a minute. The patient may lose consciousness for a few minutes. In one half of our cases an urticarial eruption, generalised over the body, or limited to the face, appeared with these symptoms. Later the pulse may become very rapid or thready; the skin becomes cold and clammy, and the patient's condition is indeed grave. In from 15 minutes to an hour a chill occurs, followed by a high fever, a temperature of 103° to 105°, and the patient may become delirious. Jaundice may occur later. The macroscopic appearance of hæmoglobinuria is almost constant."

The hæmolytic reaction may be directly fatal or it may lead to death indirectly from suppression of urine. Baker and Dodds[1] have demonstrated the factors which give rise to anuria by some very lucid experiments. Anuria is produced by the blockage of the renal tubules with precipitated blood pigment. Precipitation only occurs if the urine is acid and concentrated. A series of experiments in vitro proved that hæmoglobin is thrown out of solution when (*a*) the reaction of the medium is not more than about pH 6, and (*b*) the NaCl content is about 1 per cent or over. If the urine is alkaline, there is hæmoglobinuria but no suppression. Thus it seems that suppression of urine could be prevented by establishing an alkaline diuresis, a safeguard which could easily be adopted before transfusions which are not emergencies. In the case now reported

there was no clinical evidence of hæmolysis; the actual transfusion was uneventful and there was no backache or jaundice.

The anaphylactic or foreign protein type of reaction is still less predictable than the hæmolytic. A fatal case has been described by Carrington and Lee.[5] The patient had pernicious anæmia. There was no history of asthma, hay-fever, or other type of protein sensitisation in either donor or recipient:

"After very careful matching with a number of donors, the patient was transfused by the citrate method with 500 c.c. of blood without any immediate reaction. One half hour afterwards, however, he developed a typical anaphylactic protein reaction with high fever, spasm of the unstriated muscles, asthmatic symptoms in the lungs, involuntary voiding of urine, and several bowel movements. This subsided after one hour, but the man developed acute œdema of the lungs and died eight hours after the transfusion. During the reaction the urine was examined and no hæmoglobin found. The blood showed no hæmolysis or agglutination."

Severe foreign protein anaphylactic reactions seem to be very rare. In the majority of the cases the symptoms are limited to dyspnœa, cyanosis, swelling of the face, and urticarial rashes, and they respond to treatment with adrenalin or morphia. Doan[7] suggests that many of these reactions are due to incompatibility of the white cells. On exposure to an incompatible serum or plasma the white cells undergo vacuolation and disintegration. In Doan's series of 16 transfusions, there were 11 in which both red cells and white cells were compatible; no reaction occurred. There were four in which the donors were incompatible only as to the white cells; severe reactions followed, one proving almost fatal. In the remaining case the white cells were compatible but a severe reaction occurred; re-examination showed that the patient was an atypical group II., and ten different donors were tried before one could be secured with whose red blood cells there was not agglutination in vitro. Doan tests the white cells for compatibility by a modification of the "supra-vital" technique, and this requires much practice before reliable results can be obtained. Other factors which have been considered responsible for these foreign protein reactions are the use of new rubber tubing, excessive acidity or alkalinity and bacterial contamination of the diluting fluids, the presence of small thrombi in the blood, agglutination of the red cells, agglutination and degeneration of the platelets, and the presence of toxic substances in the plasma. Reactions are probably more frequent with the citrate technique than with the direct method. Some of the refinements suggested would remove blood transfusion from the sphere of practical medicine. There is no doubt that the frequency of reactions can be greatly reduced by familiarity with the method employed and rapid working.

The treatment of suppression of urine following hæmolysis is a difficult problem. The experiments of Baker and Dodds indicate the value of alkalis in the prevention and the treatment of this complication. Bancroft[2] has reported a case of anuria following blood transfusion in which recovery occurred after decapsulation of the kidneys on the tenth day. Osman[10] states that suppression of urine is usually accompanied by acidosis, and he has had good results by giving alkalis until the urine becomes alkaline. Very large doses of alkali are sometimes necessary. One of his patients received 1440 grains of a mixture of equal parts of sodium bicarbonate and potassium citrate in 24 hours. Where it is impossible to give alkali by mouth, he advises a drachm of the mixture in a pint of water intravenously. Our own experience with potassium citrate was not a happy one. It produced vomiting when given by mouth, and tetany developed after the intravenous injection of grs. 60 in 24 hours. As the plasma bicarbonate on the following day was only 33·6 volumes per cent. it is difficult to believe that the tetany was due to alkalosis. It may have resulted from the combination of the citrate with the calcium of the blood. It was easily controlled by the injection of calcium chloride.

In concluding this report I should like to repeat that the experimental evidence of the value of alkalis in the prevention of suppression of urine after transfusion is so clear that, except in emergencies such as acute hæmorrhage, the operation should not be carried out until alkalis have been given in sufficient dosage to render the urine alkaline.

Summary.

(1) A fatal hæmolytic transfusion reaction is described. Preliminary grouping and cross-agglutination tests had shown no incompatibility. (2) The direct mortality of blood transfusion is about 1–2 per 1000. Accidents can be minimised by careful grouping and cross-agglutination, but a certain risk is unavoidable. (3) The commonest cause of death is suppression of urine from hæmolysis and hæmoglobin infarction of the kidneys. Alkalis are recommended for the prevention and treatment of this complication.

I wish to thank Dr. A. E. Clark-Kennedy for permission to publish this case, and Prof. H. M. Turnbull for the pathological details.

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RECENT STUDIES IN THE BIOLOGY OF THE CANCER CELL.

BY PROF. A. H. ROFFO,

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THE one incontestable fact that emerges from the vast bulk of cancer literature is that the cell and its products dominate the neoplastic process, and that physical chemistry will have to clear up the mystery of the cancerous cell. Every cell which uses energy at the expense of its nutritive material does so by oxidation or by excision. In the first case the process leads to the formation of carbon dioxide and water, while in the second case it causes the formation of intermediate bodies. In oxidation there is a complete utilisation of the energy contained in the molecule of the carbohydrate, while in the second case energy is not liberated. Warburg [1 2] showed that cancerous cells have a similar action on glucose to that of lactic ferments. Normal cells produce lactic acid only in asphyxia, while neoplastic cells always produce it even when freely supplied with oxygen. Warburg aptly compares the metabolism of the tumour cell with that of a normal asphyxiated cell. The lactic acid produced hourly by a piece of rat sarcoma in Ringer solution with glucose is equal to ¼ per cent. of the weight of the tumour. Glässner [3] showed that the injection of glucose into animals with tumours produces an elimination of lactic acid in the urine, which does not happen in normal animals. Freund and Revesz have proved that it is possible to modify the speed of production of lactic acid by insulin, while Woglom has accelerated the development of tumours by adding carbohydrates. These experimental results explain a very common clinical observation—the rapid development of tumours in diabetics. On the

other hand, Correa and I [4] have observed the presence of insulin in tumours, a result which seems paradoxical.

The fermentative process, therefore, predominates in the carbohydrate metabolism of the cancer cell, and undoubtedly bears a close relationship to the cell respiration. Woglom and Russell [5] showed in 1921 that oxidation is less complete in neoplastic cells than in normal ones; the more rapid the evolution of the cell the more active its respiration. Neuschloss and I,[6] studying the influence of certain ions and venoms on the respiration, found that prussic acid and other similar substances which exercise an inhibitive action on normal cell respiration have no influence on neoplastic tissue. Adrenalin increases the reduction of the normal cells and diminishes that of the neoplastic; thyroidin acts in the opposite way. The ions Rb, SeO_3 and SeO_4 increase the respiration of adult tissues and diminish that of embryonic or neoplastic cells. We also found that the serum of cancerous animals and patients had an increased reducing power [7] proportionate to the evolution and development of the tumour. Catalysis was less in cancerous than in normal tissues, but the content of glutatium, a body which regulates the mechanism of organic oxidation, is greater in the tumour than in the normal organs. Robin [8] believes that cancer is the result of a ferment, which breaks up protein. Neuberg, Blumenthal, and Wolf mention that the endo-ferments of the neoplastic cell act not only on the protein of the tumour, but also on that of the surrounding cells. Abderhalden [9] and his school found that polypeptids of neoplastic cells are attacked differently from those of normal cells. Tumour tissues have greater lipolytic action on esters than normal tissues. Pregnancy, it may be noted, produces a physiological state with biological reactions similar to those provoked by tumours (Abderhalden).

The Ionic Composition of Neoplastic Tissues.

Investigations undertaken in this Institute [10] show a much higher content of lipoids and especially of cholesterin in neoplastic tissue than in normal tissues. This indicates an accumulation, which depends on various factors; a very important one is the accelerated development. Further investigations showed a disturbance of the nutritive metabolism of the cancerous cell. Cholesterin [11-17] is increased in the serum of cancerous animals and patients, and especially in the tissues of sarcomas and carcinomas, rising sometimes as high as 10 g. per cent. of dry material. The tissues of the animals show values which oscillate between 1 and 1½ per cent. Moreover, the metabolism is balanced by a greater activity of the cholesterinogenic organs. Even in precancerous lesions the cholesterin content is two or three times as great as in healthy tissue. The cholesterol and the water content were in many cases ten times as great in neoplastic as in normal tissues.

In consequence of these results we subjected animals to various kinds of lipoid-free diet. The animals fed on carbohydrates and small quantities of protein with absolutely no fats did not develop tumours, and tumours already present became necrotic in the first few days and later disappeared completely. It is obvious that destruction of such an important element as lipoid must profoundly alter the vitality of a cell. The cell membrane is a colloid, and cholesterin is an important regulator of the permeability of the membrane.

Meyer and Schaeffer [18] showed that in a mixture of lipoids and cholesterin the latter renders lipoids penetrable by water, and so diminishes the restriction of inbibition which determines the fatty acids. The more cholesterin there is in a gelalbuminoid mixed with lipoids the more water will it imbibe. This explains the enormous proportion of water—in certain cases 80 or even 90 per cent.—found in the tumours of rats, which are very rich in cholesterin. This percentage is only reached by embryonic tissues, which have such a close relation to neoplastic ones.[19] Is this hypercholesterinia a product of synthesis in accordance with the function of development, or is it a phenomenon of nutrition by absorption of the membrane of the cell? I have shown [17] that there is also a hypercholesterinia in embryonic tissues proportionate to their degree of development. In a culture of normal heart tissue we observed, after 48 hours, a depletion of the cholesterin of the medium by 2·06 and 8 per cent., while in cultures of neoplastic cells this diminution of cholesterin reaches very high values —59 to 83 per cent. These results show the close relationship between the development of the cells and the adsorption of cholesterin.

Certain ions,[20 21 22] especially potassium and calcium, act as regulators of the development of the tissues.[23 24 25] Wolf has obtained a retardation or acceleration of development of transplanted tumours according to which elements were in excess. Theis and Benedict found an increase of potassium in the blood of patients suffering from cancer with rapidly growing tumours. Our determinations on adult embryonic and neoplastic tissues have shown a relation between the potassium and the activity of development. We have observed a correspondence of the K/Ca relation [26] to the development of the tumour. If the value is 6·54 in tumours at the most active stage of their development it will be 3·56 in tumours in which the rate of development has decreased and which have zones of tenderness. The variations are almost entirely in the potassium; the calcium is present in nearly equal quantities in all cases.

We have observed variations which show that the conductibility of the normal and neoplastic tissues is specific and much greater in the tumour than in the normal spleen, liver, and other organs. We attribute those differences to the action of the electrolytes, especially the potassium, the amount of which varies according to the tissues. We have noticed a similar phenomenon with zinc, which Delezenne regards as an essential cellular constituent. The amount of it present in a tumour varies proportionately with the period of development. The zinc contained in these tissues is not dialysable, and must therefore be present in the form of a protein compound; this conforms with the investigations of Delezenne, who proved that the more proteins snake-venom contains the more zinc there is present.

We have demonstrated the influence of these ions on the development of tissues in vitro.[24] It was necessary to use very high dilutions of calcium to secure development. The results obtained by Zwaardemaker and Campbell and Wood suggest that potassium emits beta rays. The former noticed that the radio-active effect of calcium was to retard growth.

Summary.

The biology of cancer concerns two factors: one inherent in the cell and the other depending on the "terrain." The modifications in the evolution of the tumours in accordance with biological alterations of the "terrain," differences in the chemical compounds, the colloids, and so on, attribute special importance to this factor; but we must ask whether the chemical alterations of the tissues and their hormones prepare the "terrain," or whether the modifications are a consequence of the altered biology of the neoplastic cell. In the solution of this question lies the better understanding of the precancerous state.

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Clinical and Laboratory Notes.

A CASE OF CEREBRAL SYMPTOMS FOLLOWING VACCINATION.

RAPID RECOVERY AFTER INTRATHECAL INJECTION OF POST-VACCINAL SERUM.

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IN the report of the Committee on Vaccination presented to the Minister of Health in July, 1928, are to be found these words (pp. 200–201):—

"The occurrence of post-vaccinal nervous disease, however seldom it may occur, is of serious import and cannot fail to have an effect on vaccination both in its administrative and in its purely medical aspects. We have pointed out the extreme rarity of such manifestations, particularly after revaccination, and after primary vaccination in early infancy. Early infancy remains therefore the time of choice for primary vaccination.

"We are of opinion that only publicity among medical circles of the knowledge and experience relating to such cases as might occur in the future, both in this country and abroad, will ensure the accumulation of clinical and epidemiological data and at the same time aid the prosecution of special researches devoted to the solution of this problem."

It is in deference to this injunction that the following case is now put on record.

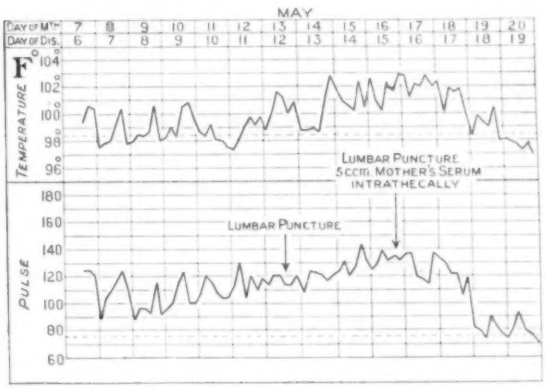
The Case Described.

A. B., a boy aged 4½ years, was brought to the casualty department of St. Bartholomew's Hospital on May 2nd, 1929. The mother stated that four days previously the child vomited, was puffy in the face and legs, suffered from headache and earache, and was found by the doctor to have a temperature of 100° F. The child was put to bed for two days, and then, seeming better, was allowed to get up, but complained of pain in the toes on attempting to walk.

In the room in which the child and his mother were waiting during the examination of the former there was also waiting another child found to be suffering from small-pox. It was therefore decided to vaccinate A. B. and his mother, and both, then and there, received four insertions of lymph. The child was then kept in an observation ward. At this time (May 2nd) there was no pyrexia. There was some general glandular enlargement, some petechiæ about the arms, legs, and back (? due to flea-bites), and the left elbow and left knee were tender on palpation and painful on movement. The tonsils were large and red. There was an apical systolic bruit and the apex-beat was displaced slightly outwards. The urine was free from albumin and blood.

The vaccination took well and the temperature rose on the sixth day (May 7th). On the eighth day the child became drowsy, and on the eleventh day he was stuporous. He vomited on this day. The limbs were entirely flaccid, but there were no pareses and no ocular palsies. (For temperature and pulse-rates see chart.) A lumbar puncture on the twelfth day yielded 10 c.cm. of cerebro-spinal fluid; Fehling reduction within the usual limits, total protein 0·03 per cent., red blood cells 52 per c.mm., white cells 4 per c.mm. (? a little admixed blood). The blood leucocytes were 8400.

The stupor and hypotonus continued on the thirteenth–fifteenth days (knee-jerks natural, flexor plantar response.) On the fifteenth day the lumbar


MAY
Day of Month 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Day of Dis. 6 7 8 9 10 11 12 13 14 15 16 17 18 19
TEMPERATURE
F° 104 102 100 98 96
LUMBAR PUNCTURE 5 ccm. MOTHER'S SERUM INTRATHECALLY
PULSE
180 160 140 120 100 80 60
LUMBAR PUNCTURE

puncture was repeated and, on Dr. Mervyn Gordon's suggestion, 5 c.cm. of the mother's serum was slowly injected intrathecally. The child's cerebro-spinal fluid was again normal on this occasion. On the seventeenth day the stupor lessened, and the child wept naturally. Hypotonus were still present. On the nineteenth day the child was more lively and the improvement in the mental state was thenceforth rapid. On the twenty-sixth day he talked for the first time since the cerebral symptoms began. A serum rash developed on the twenty-seventh day (twelfth day of injection). The subsequent course of the illness was uneventful save for a rise in the pulse-rate, which fell on getting the child up.

The mother's vaccination took well. She had been vaccinated once before, during infancy. She lost her sense of taste and smell for three weeks after the onset of her vaccinal symptoms, but she had no other nerve symptoms.

Discussion.

It is to be noted that in this child vaccination was undertaken during the late stage of some infection of unknown nature. There is therefore some suggestion that the virus of the vaccinia may have activated another virus, and that the cerebral symptoms may have been the result of the combined vira. If so, the case conforms to the third of the three possible explanations, offered by the Committee above referred to, of the occasional occurrence of encephalitis-like symptoms following vaccination.

It cannot, on the other hand, be safely inferred that the cerebral symptoms were due to the virus of the original disease alone, because the striking effect of the mother's serum suggests the operation of specific vaccinal antibody in this serum. Albeit the possibility that the good effects of the serum may have been non-specific must not be lost sight of. Should opportunity occur it may be that a trial of normal horse serum would lead to a similar good result.

This child received four insertions, and all of them took well. There is a suggestion here that, whether the Committee's recommendation in favour of one insertion only during infancy (with revaccination at 5–7 years and at 14–16 years), be followed or not, it should certainly be followed in all children who are suspected of recent infections of whatever kind, and in all persons at the time of their first vaccination.

Prof. A. H. Roffo: References.

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A FATAL CASE OF "POST-VACCINAL" ENCEPHALITIS.

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THE following case of a disease which is attracting considerable public attention at the present time seems worthy of record.

Story of the Case.

C. D., a maid-servant, aged 31, had for two or three years suffered from "anæmia, rheumatism, and menstrual trouble," but was able to carry out her duties. On May 22nd last she was vaccinated *for the first time*. "Government" calf lymph was used and it appears that 29 other persons, including C. D.'s mistress, were vaccinated from the same batch of phials without any ill-effect. C. D.'s vaccination "took" well and pursued its normal course, the arm was kept covered, and the dressing changed from time to time. On June 3rd, 12 days after the vaccination, she felt unwell on waking in the morning, vomited once, and stayed in bed, but as she had had similar attacks before no alarm was felt. In the afternoon she was found to be semi-conscious. On the following day, as she was unconscious and could not be roused, she was admitted to St. George's Hospital under Dr. Anthony Feiling.

On admission: Pallid, unconscious, but moved all limbs when pinched or pricked and resisted movement. The eyes were half open; pupils small and equal, reacted sluggishly to light; fundi not well seen. Reflexes: biceps, triceps, and supinators present, abdominal not obtained. Knee- and ankle-jerks brisk, plantar response flexor. Kernig's sign not present. No spasticity, no head retraction. Nothing abnormal detected in heart, lungs, or urine. Temp. 104·5° F. Pulse 120. Resp. 40.

On June 5th coma deeper. Complete flaccid paralysis of lower limbs. Incontinence. The eyes now showed a well-marked divergent squint. Right pupil larger than left and showed no reaction to light, left pupil reaction very sluggish. Knee-, ankle-jerks, and plantar response absent. Many coarse râles all over lungs. At intervals there was a fine chattering of the lower jaw with about 150 movements per minute. A diagnosis of acute encephalo-myelitis was made. Lumbar puncture was performed. The fluid was under pressure and opalescent; it was examined by Dr. E. L. Hunt who reported: "Slightly cloudy fluid containing a small contracted clot. Centrifuged deposit, blood present. An excess of leucocytes, not marked; polymorphs and lymphocytes (latter 40–45 per cent.). No organisms found. Sugar: Well marked reduction. Globulin: no excess. Albumin: opaque cloud. Cultures: sterile." Temp. 103°–104°. Pulse 100–110. Resp. 35–45.

On June 6th coma was still deeper but there was very slight response to pricks on arms and face. Biceps, triceps, and supinator reflexes present but all others absent. Slight cyanosis. Temperature, pulse, and respiration as before. Death occurred at 4.30 A.M. on June 7th, about four days after the first appearance of symptoms. Treatment had consisted of cold sponging, nasal feeding, and stimulants.

Post-mortem Appearances.

An examination made 8½ hours after death showed the body of a well-nourished woman. On the left upper arm were two healthy vaccination scabs with no local swelling or inflammation. The serous sacs contained no excess of fluid. Heart normal. Lungs: some early fibrinous pleurisy at the left base. Nodules of inactive fibro-caseous tuberculosis at both apices. Intense congestion and œdema with early hypostatic consolidation at bases. Liver congested. Spleen congested but rather soft. Kidneys: cortex cloudy, general congestion. Bladder distended with urine. Brain: some general swelling shown by flattening of the cerebral convolutions; a well-marked "pressure cone" on the cerebellum. No meningitis but the surface was everywhere intensely congested and of a cherry red colour. On section some increase of fluid in the ventricles was noted. The internal vessels were also intensely congested but no hæmorrhages were apparent to the naked eye. Spinal cord: intensely congested and somewhat softer than normal throughout its length. The other organs showed nothing abnormal.

A preliminary microscopical examination has been made of sections of the basal ganglia, crus cerebri, lumbar cord, and kidneys. No meningitis is present, all vessels are intensely congested. In all the sections foci of cellular reaction are seen. These are always related to vessels and form a scattered and rather widespread zone around them. No such foci are found apart from vessels. The cells resemble endothelial cells in size and shape and have fairly clear oval nuclei. The perivascular sheaths are as a rule empty but some contain a few cells of lymphocytic type. No polynuclear cells are seen. One very small hæmorrhage was noted in basal ganglia. In the more intense foci many of the ganglion cells show degeneration of varying degrees. Areas of demyelination of nerve-fibres were noted particularly in the section of the cord.

The kidneys showed intense congestion of the glomerular tufts and moderate congestion with a few small hæmorrhages elsewhere. The convoluted tubules showed well-marked degeneration of the epithelium in contrast to the deeper tubules which appeared healthy.

Commentary.

These findings appear to me quite consistent with those recorded in other cases of post-vaccinal encephalitis. The main points of difference from acute anterior poliomyelitis and epidemic encephalitis lethargica are:—

1. The distribution of the lesions throughout both brain and cord.
2. The foci of inflammation tend to be larger and are all related to vessels but the perivascular sheaths are practically free from cells.
3. The predominant cell is of an endothelial not a lymphocytic type.
4. The demyelination of nerve-fibres is marked.

The precise ætiology of these cases is not yet clear and I do not propose to embark upon a discussion of theories, but certain points seem to be established and to be supported by this case: (1) Encephalitis (with possibly very rare exception) follows primary vaccinations only. (2) It does not occur after unsuccessful vaccination. (3) There is no evidence that it is due to a secondary infection. (4) It is independent of the method or animal used in preparing the lymph. (5) Very young children seem to escape this complication.

I wish to express my thanks to Dr. Anthony Feiling for providing me with the clinical details of the case, and to Dr. E. L. Hunt for his report on the cerebro-spinal fluid.

ORAL IMMUNISATION AGAINST TYPHOID IN SOUTH AFRICA.

By EUSTACE CLUVER, M.D., D.P.H.,
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OF the seven million persons resident in the Union of South Africa, five and a half million are non-European, the great bulk of whom are uncivilised. This large non-European population is the reservoir from which the towns and industries of the Union draw their unskilled labour. These people in general have little conception of hygiene, and unless carefully supervised will congregate in the towns under grossly insanitary conditions. Typhoid fever, so closely associated with insanitation, is therefore rife amongst them. It is prevalent not only among natives living under urbanised conditions in close association with Europeans in the towns, but also in the kraals, where conditions are also often grossly insanitary. Many of the smaller towns have primitive sanitary services, with badly conducted, single-pail night soil systems, abundance of flies, and exposed and untreated water-supplies.

TABLE I.

Year.	Typhoid notifications.	Year.	Typhoid notifications.
1923 ..	4163	1926 ..	4454
1924 ..	3859	1927 ..	4018
1925 ..	4390	1928 ..	5787

The Union Health Department is actively engaged in improving sanitary conditions by a system of health inspections, general advice, and other propaganda. But in the meantime typhoid continues to take a heavy toll. Notifications of this disease during recent years in the Union are shown in Table I.

The actual incidence of the disease is probably very much higher than indicated by these figures. Only a small proportion of natives living in country districts consult a doctor during typhoid; and unless some circumstance, such as exceptional severity, attracts the attention of the magistrate or district surgeon such cases go unnotified. On the gold mines of the Witwatersrand the annual incidence of typhoid per 1000 natives employed, except on well-conducted, sewered mines, is seldom below unity, and on sanitarily unsatisfactory mines it is generally over 5.

Vaccination.

Although sanitation is making steady progress throughout the Union, the high incidence of typhoid has called for more direct action. Inoculation by the injection method is impracticable on a general prophylactic scale, owing to the fact that a skilled process, which can only be carried out by members of the medical profession, is involved, and to the resistance offered by natives to a somewhat painful proceeding. Natives in general are, however, curiously willing and even eager to absorb medicines ("Muti") by mouth. The method devised by Prof. Besredka of orally administering the vaccine in combination with a gall pill presented a method of general prophylaxis very acceptable to the native.

The vaccine is being prepared on a large scale by the South African Institute for Medical Research. At first it was supplied only as a suspension of killed *B. typhosus*, *B. paratyphosus* A and *B. paratyphosus* B (in much greater concentration than that used in the ordinary T.A.B. vaccine), together with pills of of ox-bile, coated with keratin in order that they might pass through the stomach undissolved and prepare the intestine for the absorption of the injected vaccine. A teaspoonful of the vaccine (well shaken before using) is administered along with one of the bile pills on each of three successive mornings before any food has been eaten. The Institute first started the routine manufacture of this vaccine in April, 1925. The suspension is still being produced and is being used for mass prophylaxis on certain mines. Since May, 1928, the vaccine has also been put up in the form of pills, and it is in this form that it is being issued to medical practitioners and local authorities. Twelve different strains are used in its preparation. Each strain is cultivated separately in broth medium for about 24 hours at 37° C. To the broth culture 0·5 per cent. formalin is added and allowed to act overnight. The medium is then centrifugalised and the sediment is dried in the incubator, after which it is ground in a grinding machine. From the powder the pills are prepared, each pill containing 0·015 g. of dried bacilli which is approximately equivalent to 45,000 million organisms per pill. Vaccine for oral administration is also being prepared, put up in pill form, by at least one private laboratory. Altogether the number of triple doses of this oral vaccine issued by the South African Institute for Medical Research up to the present is, in the form of suspension, 31,141, in the form of pills 17,154.

Experience on the Mines.

The first large-scale experiment with oral vaccine in this country was made on a Mine "A" in the Germiston area.[1] This mine has two compounds about a mile apart, one housing 1850, the other 1750 natives. A typhoid outbreak (probably fly-borne from unknown carriers, the mine using the conservancy system) commenced on the mine in November 1922. Oral vaccination was performed between Jan. 4th and 12th, about 3500 natives being vaccinated and about 100 being missed. The total number of cases admitted to the mine hospital during the outbreak was 53. Of these, 33 were admitted previous to Jan. 4th, and 20 between Jan. 4th and Feb. 24th. After that no further cases were admitted for several months. Of the 20 cases admitted after vaccination had commenced, four had not been vaccinated. The remaining 16 were admitted late in the disease, which suggests that they were in the incubation stage when vaccinated.

The great bulk of the natives employed on the Witwatersrand gold mines serve a contract of a year or less. At the end of 12 months very few of the vaccinated natives were left on this mine; and in October, 1923, another typhoid outbreak occurred in the same mine. The natives were again vaccinated and the outbreak brought to an end. Since that date all recruits arriving on this mine have been vaccinated by the oral route, and the annual incidence per 1000 has dropped from 23·3 in 1923 to 10·4, 10·1, 5·2, 4·0, and 4·7 in the succeeding five years. Though typhoid still occurs on the mine its incidence during the past three years has been low for a mine with an unsatisfactory conservancy system and generally very unsatisfactory sanitary conditions. Its present typhoid incidence compares very favourably with that of a mine ("B") in the neighbouring municipality where conditions are in every way comparable, except that routine oral vaccination is not carried out.[2]

TABLE II.—*Typhoid Incidence on Two Mines on the East Rand.**

Year.	Mine.	Cases.		Deaths.		Average number employed.
		Admissions.	Per 1000	No.	Per 1000	
1927 ..	A	13	3·98	4	1·22	3,291
	B	127	11·57	30	2·73	10,978
1928 ..	A	16	4·74	4	1·19	3,373
	B	115	9·72	46	3·89	11,826

* With similar conditions except that at mine "A" all native recruits are treated with oral vaccine.

Oral vaccination is being very strongly urged by the Union Health Department on all mines where the sanitary removal system continues to be unsatisfactory. On sewered mines typhoid has virtually disappeared, and its incidence on mines with a satisfactorily conducted dual pail system is very low.

Routine oral vaccination on sanitarily unsatisfactory mines has not caused the disappearance of typhoid, but the incidence has been very greatly reduced.

Experience of Local Authorities.

As mentioned above, sanitary conditions in some of the smaller towns of the Union, particularly among the native populations, are often grossly unsatisfactory. In such towns sanitary improvements are being urged by the Department; but in the meantime, especially in the face of an epidemic of typhoid, mass vaccination is being recommended.

In three municipalities in which the typhoid incidence was high during the year ended June 30th, 1928, mass oral vaccination was introduced early in 1928, and by the second half of the year the typhoid incidence had fallen to relative insignificance. (Table III.)

TABLE III.—*Typhoid Incidence in Three Towns in which Mass Oral Vaccination was Introduced during the First Half of 1928.*

Municipality	Cases during 12 months ended June, 1928.	Cases during 6 months ended December, 1928.
Heilbron ..	97	0
Ermelo	120	3
Bloemfontein ..	48	13

Similar results have been obtained in other municipalities where it was been possible to inoculate the bulk of the population at risk. Very good results have been obtained in Pretoria.[3]

Conclusions.

The experience on the mines and in urban areas of the Union of South Africa, although observations have not been made on strictly experimental lines (no satisfactory control experiments having been

practicable), would yet appear to indicate very definitely that the degree of immunity established by the oral method of administration of the vaccine is at least equal to that obtained by subcutaneous inoculations. The immunity appears to be established more quickly. Oral vaccination has two very important advantages; the subjects, particularly natives, are generally much more willing to take "medicine" by mouth than by injection with a needle; no malaise follows oral administration, whereas unpleasant sequelæ often occur with subcutaneous inoculation.

References.

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2. Cluver, E.: Jour. Med. Assoc. of South Africa, August, 1928.
3. Annual Reports of the Medical Officer of Health for Pretoria.

Medical Societies.

NORTH OF ENGLAND GYNÆCOLOGICAL AND OBSTETRICAL SOCIETY.

A MEETING of this Society was held at Leeds on May 24th.

Vaginal Examinations and Puerperal Infection.

Dr. A. M. CLAYE read a paper on the Puerperal Morbidity-rate in Cases Delivered Normally; a Comparison between Cases Examined Vaginally and Cases not Examined Vaginally. He said that a series of 1546 normal cases at the Leeds Maternity Hospital had been investigated, the following being excluded from the normal category: (1) all cases requiring intra-uterine manipulation or instrumental assistance during labour; (2) all cases where there was any obvious predisposing cause of puerperal sepsis—e.g. ante- and post-partum hæmorrhage; and (3) all cases of puerperal pyrexia due to definite extragenital causes. Cases with perineal tears were classed separately to avoid confusing the issue. Cases admitted to the hospital in labour from outside sources were excluded owing to lack of definite information about vaginal examinations before admission. The morbidity-rate in this class was abnormally high.

The remaining normal cases had been classified according as they were examined vaginally or not, and the puerperium had been described as:—(1) *morbid:* Ministry of Health standard of puerperal pyrexia; (2) *submorbid:* where the temperature reached 99 °F. or more at least twice during the 21 days following delivery; and (3) *normal:* all apyrexial cases, cases where the temperature never reached 99°, and cases where the temperature reached or exceeded 99° on one occasion only. The temperature was taken in the axilla in all cases.

The vaginal examinations had been done in almost all cases by pupil midwives under the supervision of the labour ward sister in order to comply with the existing rule of the Central Midwives Board, which required pupils to perform a certain number of vaginal examinations. The patient's vulva was shaved on admission, the examiner wore boiled gloves, and antiseptic precautions were observed during the examination. The results were as follows:—

CASES WITHOUT PERINEAL TEARS.

Cases Examined Vaginally, 309.

(*a*) Number morbid	.. ..	7 or 2·3 per cent.
(*b*) Number submorbid	.. ..	21 or 6·8 ,,
Total (*a*)+(*b*)	.. ..	28 or 9·1 ,,

Cases not Examined Vaginally, 778.

(*a*) Number morbid	.. ..	10 or 1·3 per cent.
(*b*) Number submorbid	.. ..	41 or 5·3 ,,
Total (*a*)+(*b*)	.. ..	51 or 6·6 ,,

The above figures showed that the total morbidity-rate was one and a half times as great for the cases examined vaginally.

CASES WITH PERINEAL TEARS, 459.

(*a*) Number morbid	.. ..	12 or 2·6 per cent.
(*b*) Number submorbid	.. ..	50 or 10·9 ,,
Total (*a*)+(*b*)	.. ..	62 or 13·5 ,,

Probably in cases examined vaginally the increased morbidity-rate was due to the finger moving infected matter from a comparatively safe position in the vagina to a dangerous position within the cervix rather than to the introduction of new organisms. Dr. Claye thought that rectal examination could replace vaginal examination except in the following groups: 1. Cases of antepartum hæmorrhage. 2. Cases where it is important to know the exact size of the os, and this cannot be gauged by the rectum; these are mainly breech presentations. 3. Cases where the doctor has been called in during labour to a patient whom he has not seen before where he cannot decide on the proper treatment without vaginal examination—cases of incompatibility between the head and the pelvis. 4. Cases where the doctor is about to resort to operative treatment. He maintained that the amount of dilatation of the os could nearly always be determined from rectal examination and that this method could also determine the presence of the bag of membranes, prolapse of the cord, and a face presentation. As far as midwives were concerned, their duties under the four indications given above (of which numbers 3 and 4 did not apply) were clear. In antepartum hæmorrhage they had to summon medical aid. In breech presentations, unless uncomplicated, they had to summon medical aid, and no one could be certain that a breech would be uncomplicated until delivery was in progress. He therefore held the opinion that it was not necessary for midwives to make vaginal examinations and that they should be forbidden to do so.

Prof. CARLTON OLDFIELD said that he considered most severe infection was conveyed from outside. He had rarely seen a case of severe infection where no vaginal examination had been made and could not recollect a case of infection where rectal examination only was used. He considered that the main danger lay in doctors and senior nurses who did general work and made vaginal examinations.

Mr. WILLIAM GOUGH said that in Leeds Maternity Hospital they had given up lysol for biniodide and only allowed rectal examinations. In Berne it had been found that this halved the morbidity-rate in the Berne Maternity Hospital, and this institution refused to admit patients who had been examined vaginally outside.

Dr. W. W. KING (Sheffield) said that he had analysed 457 of his own cases. Fifty-five had been examined vaginally and of these one was morbid (1·9 per cent.), but this patient had had a manual removal of the placenta. Four hundred and two had been examined rectally only; of these two were morbid (0·5 per cent.). He considered this group of vaginal examinations too small to be of much value, but using Dr. Claye's classification the one morbid case in this group would be excluded on account of the interference necessary and therefore there would be a higher morbidity-rate with rectal examinations. He pointed out therefore that figures alone could be made to show anything.

Mr. WILLIAM GOUGH showed a specimen of

Hyponephroma of the Ovary.

The patient was a married woman aged 25. She had been normal as a child. When seen she had a deep bass voice and had to shave daily. The menses had appeared at the age of 13 and were regular up to the age of 20 when they ceased, and the changes in secondary sex characteristics began to appear. Her sexual feelings were normal. A mass, separate from the uterus, was found in the left iliac fossa and there was some free fluid. On August 25th, 1928, abdominal section was performed. Two or three pints of straw-coloured fluid escaped and a tumour of the left ovary, which had no adhesions, was removed. It was of a bluish colour with pinkish orange excrescences on its surface. The right ovary and uterus were normal and there were no swellings in the kidney regions. The tumour was reported as a typical hypernephroma.

Twenty-eight days after operation (said Mr. Gough)

the menses appeared. They next occurred a fortnight later and thereafter were regular. As the patient had last menstruated on April 6th, 1929, she might now be pregnant.

Dr. CLARA STEWART said the tumour was a simple benign hypernephroma exactly similar in structure to an adenoma of the adrenal gland.—Dr. LEITH MURRAY (Liverpool) asked if male characteristics occurred with unilateral renal hypernephromas, and said that he thought Glynn asserted that they only occurred with bilateral tumours. He (Dr. Murray) had seen a case of sudden change in sexual characteristics in a woman aged 25 in whom no abnormalities in pelvis or renal areas could be found. He asked if the cells in this case could be paralutein cells.—Dr. STEWART said she did not consider that the cells showed the characteristics of paralutein cells. It was not necessary for the tumours to be bilateral to cause changes in sexual characteristics.

Miss RUTH NICHOLSON recorded two cases of

Pyometra.

The first patient was a single woman, aged 49, whose chief complaint was a constant vulval irritation for four to five years and more recently a vaginal discharge. She had had cystitis as a child. The periods commenced at 14 and had always been irregular and scanty. She had not menstruated at all for the last five years. On bimanual examination thickening and fixation of the appendages was felt and a diagnosis of tuberculous salpingitis was made. At operation very marked adhesions were found. The tubes were nodular, closed, and adherent to the ovaries. Panhysterectomy was performed. When the uterus was opened the cavity was found to be filled with a thick yellow pus. Microscopical sections showed typical giant-celled systems.

The second patient was a woman, aged 70, who had had a high amputation of the cervix eight years previously. She complained of a yellow discharge, partial rectal obstruction, and some vaginal hæmorrhage. A mobile, solid mass about the size of an orange was felt continuous with the cervix. At operation the uterus broke away, at the point where the previous amputation had been done, as soon as the vessels and cellular tissue had been cut across. The specimen showed the uterine cavity distended with pus and lined with granulation tissue. Microscopically there was no evidence of malignant disease.

Dr. D. W. E. BURRIDGE recorded a case of

Puerperal Infection with Bacillus welchii.

The patient was a primipara, aged 39, admitted to hospital with a diagnosis of prolonged labour and vomiting. Labour began on March 21st, 1929, and on admission on the 25th her general condition was good (temp. 98·4° F., pulse 88). Vomiting had ceased, no pains were present, and the uterus was not tender. No fœtal heart sounds could be heard. The cervix was 5 shillings dilated but not fully taken up.

There was no change on the 26th, but by the morning of the 27th she was seriously ill, restless, of toxic appearance, and with a rising pulse. By noon the pulse was 120, the abdomen was distended, and the uterus tender. Preparations were made to assist the uterus to empty itself. The cervix was now half dilated and an unsuccessful attempt was made to dilate it manually. This manipulation allowed the escape of a quantity of highly offensive gas, and some foul, frothy brown fluid. As immediate evacuation of the uterus was inadvisable axis-traction forceps were applied and a weight of 7 lb. was attached to the traction rods over a pulley. Pituitrin, 4 minims, was given at ½-hourly intervals for five doses. These measures were successful and by 5 P.M. the child's head was born. There was considerable difficulty with the delivery of the trunk owing to the enormous gaseous distension of the abdomen. After delivery there was a free escape of browny frothy fluid and much gas but no hæmorrhage. Swabs from the interior of the uterus, umbilical cord, and fœtal abdomen gave a good growth of *B. welchii*. The patient stood delivery well but in the evening restoratives were necessary. On the next morning she was a little better but the placenta was still in the uterus. It was left alone as it was not causing symptoms.

On March 28th 10 c.cm. of Weinberg's anti-gas-gangrene serum and 40 c.cm. antistreptococcal serum were given. Further doses of anti-gas-gangrene sera were given on the 2nd, 3rd, 4th, 5th, 6th, 8th, and 11th days of the puerperium. Attempts to express the placenta on the 4th and 5th days of the puerperium were useless but very painful. The patient remained in extremis for four days after delivery and a change was then noticed; once this was manifest the progress towards recovery was remarkable, despite a vesico-vaginal fistula which became manifest on the 6th day. By the 17th day the uterus was down to the pubis and the lochia were scanty and non-offensive. The patient was sitting up on the 21st day and walked a few steps on the 35th day.

The main points of the case (said Dr. Burridge) were: (1) the absence of hæmorrhage; (2) the fact that the placenta was never recovered would suggest that it was liquefied; (3) the retained placenta might have prevented the spread of infection; (4) the value of anti-gas-gangrene serum.

Dr. E. O. CROFT remarked on another case in which a weight and traction rods were used to secure delivery.

Prof. OLDFIELD mentioned a case of full term ectopic pregnancy in which the child was extracted but the placenta never came away. Later this patient had an operation for ventral hernia and no trace of the placenta could be found.

Dr. J. E. STACEY (Sheffield) commented on the method of delivery as being useful in cases where there were no pains, and a dead child, in the presence of infection of the mother.

Dr. KING had had three cases of *B. welchii* infection, in none of which the patient had recovered. He thought the conduct of labour in this case had been admirably conservative. The idea of forceps plus a weight was valuable, but it had its dangers, as witness the vesico-vaginal fistula in this case. In his opinion labour ceased because there was an œdema of the uterine muscle which caused paralysis. He had had a case in which he left the placenta in situ and on the 10th day a piece about the size of five shillings was passed and that was all. He considered that in the presence of a gas-forming organism tissue destruction must be much more rapid.

Dr. MURRAY had seen two cases of gas-gangrene infection both of which were fatal. The distressing feature he noticed was that the patients were acutely conscious to the end.

Dr. BAILEY had seen a number of cases of retained placenta. He always left the placenta alone in the absence of symptoms. Altogether he had had about 30 cases and quoted some in which the placenta came away at varying intervals from 30 hours to 6 days, and one case where the woman would not allow him to examine her or see the lochia. In this case, to the best of his knowledge, the placenta never came away. She was seen in his surgery two months after her confinement, quite well.

Prof. CARLTON OLDFIELD reported two cases of

Entero-vesical Fistula.

The first patient was originally seen in 1914, when a diagnosis of diverticulitis was made and a pelvic abscess drained by posterior colpotomy. In 1928 the patient had three attacks of pain at different times, and after the third attack began to pass fæces and flatus from the bladder. This made the speaker still more certain that the condition was diverticulitis. The patient now had so much trouble that something had to be done. No information was obtained from cystoscopy. Abdominal section was performed and very dense adhesions found. Eventually the bladder, uterus, and sigmoid were separated, and a stony hard swelling was found adherent to the uterus and sigmoid. This was eventually separated, leaving a hole in the sigmoid and a track lined by granulation tissue was found leading down to the bladder. The track was scraped and the hole in the sigmoid closed. The patient later developed obstruction which was relieved by a cæcostomy and thereafter she made a good recovery. The report on the nodule was "typical, caseating, active tuberculosis; some parts of ovary, and plain muscle are present." Prof. Oldfield thought that the original lesion must have been tuberculous salpingitis. The second case was one in which a vesico-vaginal fistula followed a Wertheim's operation. The fistula was repaired and a few days later urine was being passed per rectum. No further treatment was undertaken for this patient and she remained quite well. Her only disability was the necessity for frequent bowel actions to pass urine.

Reviews and Notices of Books.

PATHOLOGY.

Pathology for Students and Practitioners. Authorised translation of the "Lehrbuch der Pathologischen Anatomie." By Dr. EDWARD KAUFMANN, Professor of General Pathology and Pathological Anatomy, University of Gottingen. Translated by STANLEY P. REIMANN, M.D., Pathologist and Director of the Research Institute of the Lankenau Hospital, Philadelphia. London: H. K. Lewis and Co., Ltd. 1929. 3 vols., pp. 2452. £6 6*s*.

Kaufmann's "Lehrbuch der Speziellen Pathologischen Anatomie" has long been recognised as the leading work of reference in this subject, and an English translation has been overdue. Dr. Reimann has performed his task in a manner to earn him the gratitude of English-speaking pathologists. The original text has been faithfully reproduced and any editorial interpolations are clearly indicated. Kaufmann has always been one of those teachers who recognised the need of emphasising constantly the close connexion between pathological anatomy and the practice of medicine, and clinical observations and problems are given more sympathetic consideration in the text than is customary in some of the classical works on pathology. The translator reflects the impetus given to the study of pathological anatomy by the discovery that what he calls "pathological physiology" cannot progress without familiarity with structural lesions or without the experience, not easily acquired, which alone enables any individual lesion to be properly classified. The chapter on the blood lymph and hæmatopoietic organs is less satisfactory than most of its neighbours. This is possibly because hæmatology has been the subject of so many excellent monographs that any text-book account now seems inadequate. On the other hand, the 250 pages devoted to the respiratory organs, in which section the thymus and thyroid glands are included, are peculiarly lucid and informative. Prof. Kaufmann regards a severe inflammatory œdema of the lung as the most common cause of death in poisoning by war-gases. The translator adds a note recording evidence in favour of the opinion that, if recovery takes place, little or no permanent injury results, and that gassing has little or no effect on subsequent pulmonary tuberculosis. The pathological importance of an enlarged thymus gland is not assessed. The hasty diagnosis of status lymphaticus in face of sudden death is deprecated, but it is admitted that no more satisfying explanation has been put forward.

Over 100 additional drawings have been provided for this edition, which is beautifully produced. The individual student will probably find the price prohibitive, but as a work of reference it should be in every pathological laboratory and library.

A Text-book of Pathology. Fourth edition. By W. G. MACCALLUM, Professor of Pathology and Bacteriology, Johns Hopkins University, Baltimore. London and Philadelphia: W. B. Saunders Company. Pp. 1177. 45*s*.

THE fourth edition of this well-known text-book has been thoroughly revised and partly rewritten. The subject of pathology has become so vast that no individual can claim first-hand knowledge of all its branches. For this reason Prof. MacCallum has omitted or contracted certain sections which appeared in previous editions. Chapter X., for example, which deals with fever and immunity, has been rigidly cut down; the section dealing with the mechanism of the maintenance of the acid-base equilibrium of the body has been deleted; and the phenomena of immunity are dealt with in only the briefest way. In Chapter XIII. the section dealing with the pathology of the conduction bundles of the heart no longer appears. To compensate for this pruning other portions of the book have been enlarged, and the general revision has also included the illustrations. The text-book was conceived on original lines, and its distinctive characters have been maintained. It has always had a wide public, and will continue to appeal to those who appreciate a logical and philosophical presentation of pathological principles and facts.

Principles of Pathology. For Practitioners and Students. By H. D'ARCY POWER, M.D., F.R.P.S., Professor of Pathology, College of Physicians and Surgeons, San Francisco; and WILLIAM W. HALA, M.D., Assistant Professor of Pathology, Long Island College Hospital, Brooklyn, N.Y. London and New York: D. Appleton and Co. 1929. Pp. 787. 42*s*.

Since there are already several sound text-books on pathology in the English language, it is natural to look for any special features or reasons which shall justify the publication of any new contribution to this branch of medical literature. In their preface to this work the authors suggest that though the existing text-books present current knowledge accurately and in detail they do not sufficiently concentrate on the essential and important, and therefore do not meet the requirements of men studying the subject for the first time, or of practitioners who have need to refresh themselves on points long forgotten, or in regard to recent discoveries.

Whether it is possible or even desirable to combine in a single volume a broad presentation of pathological principles such as a student beginning the study of the subject may be presumed to need, and the detailed information necessary in a work of reference, is a matter of opinion. By careful selection and avoidance of rare and disputed details the authors have covered a very wide field, but they cannot be said to have achieved a striking success. The book proceeds along conventional lines, except that the section index is adopted in preference to the page index system, but often enough the authors appear to say too little or too much. The principles of pathology and the modern trend of experimental work are not emphasised as they should be in a book intended for the use of students. In the section on tumours, for example, there is no mention of the experimental investigation of malignant disease beyond a reference to the work of "Gage and Barnard." On the other hand, the detailed descriptions of individual lesions are often so scanty as to be actually misleading. In Section 284, for example, it is stated that ulcero-membranous stomatitis is caused by the spironema vincenti, "a bacterium which occurs in two forms, a fusiform bacillus and a short spiral type." Again, in Section 829, dealing with neoplasms of the ovary, the authors write as follows: "A peculiar tumour of mixed sarcomatous and carcinomatous structure has been described by Krukenberg and others, and is usually designated as the Krukenberg tumour. There is usually a history of primary gastric carcinoma. It may extend into the peritoneal cavity." These examples, and many others could be quoted, illustrate the difficulty of simplifying a work of reference and are not brought forward in any carping spirit. It is possible that the authors may be correct in both statements, but such important principles are involved that if further explanation is impossible it would be better to omit them.

This text-book is well written, and though it has its defects it has features which will no doubt ensure it a public. There are upwards of three hundred illustrations, several in colours; the majority of them are good, but some have been simplified beyond the limits of usefulness.

OBSTETRIC FORCEPS: ITS HISTORY AND EVOLUTION. By KEDARNATH DAS, C.I.E., M.D., Professor of Midwifery and Gynæcology, Carmichael Medical College, Calcutta. Calcutta: The Art Press. 1929. Pp. 903.

FOR some 12 years Prof. Das has been carrying out an investigation into all that appertains to the

obstetric forceps. His object is to produce a comprehensive treatise on this subject, and the volume under review is only the first result of his inquiry. It contains the history of the evolution of obstetric forceps, followed by a detailed description of various patterns. The more practical points have been left to a further volume or volumes to be published in the future. Over two thousand references have been consulted, 920 of which have provided the material for the present volume. It is full of quotations and literal translations, particular attention being paid to one of the earliest monographs on the subject, that by Mulder written in 1794.

The first section is largely concerned with the vexed question as to who was the original inventor of the obstetric forceps for use as a conservative instrument. The author has analysed all the early writings he has been able to discover and, although many "forceps" are mentioned they all appear to have been instruments for delivering a dead and not a living child. In this section the history of embryotomy is dealt with in considerable detail, and numerous curious instruments are illustrated. Although many writers, including Partridge in 1905, deny that the Chamberlens invented obstetric forceps, Prof. Das seems to hold that all previous instruments were used solely as craniotomy forceps. Partridge gives the credit to Rueff, but, although Rueff had the idea of using his instrument on the living child, the application of his actual instrument to this purpose would have been a difficult if not impossible feat. A section is devoted to the history of the Chamberlen family. Their conduct in concealing their discovery from their brother practitioners, the author says, has been much criticised but, unprofessional as it may seem to the present generation, their attitude was, according to Prof. Das, quite in keeping with medical ethics of their day.

The remainder of the book is devoted to illustrations and descriptions of the 550 varieties of the obstetric forceps discovered by the author. Several tables have been compiled to show their chronological order, the principles of their mode of action, and their measurements. A short, quite amusing chapter gives references to the obstetric forceps in allegory, literature, and art.

ALCOHOL AND HUMAN LIFE.

By COURTENAY C. WEEKS. London: H. K. Lewis and Co., Ltd. 1929. Pp. 201. 3*s*. 6*d*.

Dr. Weeks originally contemplated a complete new edition of Horsley and Sturge's "Alcohol and the Human Body." This worked out to an impracticable size, so he has done what is probably more useful and issued an up-to-date addendum to that book which, at its modest price, should have a wide circulation among those interested in social problems. He sets out to describe the effects of alcohol on the body, which are often hard to demonstrate beyond cavil. It is, indeed, generally impossible to be sure whether any pathological condition or death which is associated with alcohol is due to the direct action of the drug on the tissues or to the general deterioration of character and standard of life which its habitual use entails. It is probably also true to say that the mental and spiritual effects of alcohol are far more serious than its objective bodily injuries, though it is extremely difficult to disentangle one from the other. Those, however, who doubt the far-reaching influence of alcohol on mortality should read Chapter IX., which summarises the impressive facts of occupational death-rates set out in the Decennial Supplements; the drink trade is a fearfully dangerous occupation. Throughout Dr. Weeks makes his points with an enthusiastic conviction that alcohol is wholly evil. It is permissible to suggest that he might with advantage in places have been a little more critical. The chapter, for instance, on the blood and circulation is quite unconvincing; if alcohol has some small effect on blood calcium is there any serious reason for thinking that any substantial harm is done thereby? Perhaps bread and milk or a coffee-ice-cream-soda would do the same. And such a statement as (p. 62) "the influence of alcohol on the skin is also evidenced in a disease called pellagra" is true only in the sense in which we may talk of alcohol as being a cause of lousiness or any other state arising out of a debased standard of life. A little more discretion would have given fewer chances to hostile critics. On p. 14 there is a considerable misprint: toxic for tonic.

GROWING OLD GRACEFULLY.

By LEONARD WILLIAMS. London: Jarrolds N.D. 1929. Pp. 48. 1*s*.

WORK hard, eat little, be in the open air as much as you can. Could any sound rules be simpler or more sane? In a preface Lord and Lady Aberdeen add another which is not quite so easy—marry the right person. In these days of silly fads, Dr. Williams deserves special thanks for his sensible little book.

GENERAL BIOLOGY.

Vie et reproduction. By MAX ARON. Paris: Masson and Co. 1929. Pp. 366. With 190 figures. Fr.38.

Prof. Aron has written an admirable survey of such general biology as all students of medicine, young or old, should be acquainted with. There has been much progress in recent years, and we know of no book which will so well acquaint those whose main interests lie in other fields with what has been going on. The first part deals with cells—their structure, movements, multiplication, and differentiation. The second part discusses the organism as a whole, the humoral and nervous correlations and the principles of growth. In the third part (which is equally well covered in many recent books) we come to sex, sexual characters, and heredity. The illustrations are excellent and a senior medical student who studies the book will derive great practical advantage.

A EUROPEAN FLORA.

Illustrierte Flora von Mittel-Europa. By Prof. GUSTAV HEGI. Munich: J. F. Lehmann.

THE magnificent illustrated flora of Central Europe produced under the editorship of Prof. Hegi of Munich is now approaching completion. Three volumes had appeared before war broke out in 1914, when the issue was suspended, and it seemed likely indeed that the publication would never be completed. Now, however, nine other volumes have been issued, completing the work with the exception of a separate index volume, which is promised in the course of the year. The twelve volumes contain something over 7000 pages of text, with 280 plates, mostly in colour, and some 4250 illustrations in the text. The whole is a mine of information on the morphology, anatomy, biology, and distribution of all varieties of flowering plants which occur, commonly or rarely, in Germany, Austria, Switzerland and the adjoining countries. The work will appeal not only to the scientific botanist, for under each species are included notes on the history of the plant, its soil and cultivation, its varieties, the pet names by which it is called in various parts of the country, the disorders to which it is subject, the uses to which it has been or may be put in industry and the arts, and much else. For example, the second half of Volume VI., which completes the natural order Compositæ, contains much curious information about the *Artemisia absinthium*, known in German as *Wermut*, from which wines and bitter cordials have been prepared since the dawn of history and which was prized by Galen for fevers, by Paracelsus for malaria, by Hippocrates for chlorosis, and by the editor of the present volume for the relief of thirst, which is achieved by the mere smell of the fresh plant. Some of this information could no doubt with care and toil be found elsewhere, but there is no other work with so many coloured pictures of individual flowers, while the photographs

in the text illustrate the habitat and associations of the plants described. The English botanist will find included a large proportion of his native flowering plants and grasses as well as the alpine and sub-alpine species with which he meets on his holiday tours. Obviously no public library would be complete without a copy of this work, and to any lover of flowers it will afford a never-ending source of enjoyment. The total cost up to date of the twelve volumes in paper covers is 369 marks, or bound in linen boards 406 marks, and it is understood that the price will be raised as soon as publication is complete.

PEDIATRICS FOR THE GENERAL PRACTITIONER.

By H. M. MCCLANAHAN, M.D., Professor of Pediatrics, University of Nebraska. London: J. B. Lippincott Company. 1929. Pp. 606. 25s.

THIS book differs in some respects from the majority of pediatric text-books of similar size; it is written for general practitioners rather than students, and deals fully with practical points of diagnosis and treatment while little space is devoted to pathology. It is profusely illustrated by photographs and radiograms. A praiseworthy amount of attention is paid to the characteristics of the normal child, and to the details of breast feeding. The author believes that the degree of attention which has been focused upon complicated methods of artificial feeding has led to some neglect of breast feeding. He includes a short description of percentage feeding. The common disorders of childhood are treated clearly and practically, though the distribution of space is somewhat uneven. Rickets, for instance, is treated too briefly, and no mention is made of irradiated drugs. On the whole the book is satisfactory.

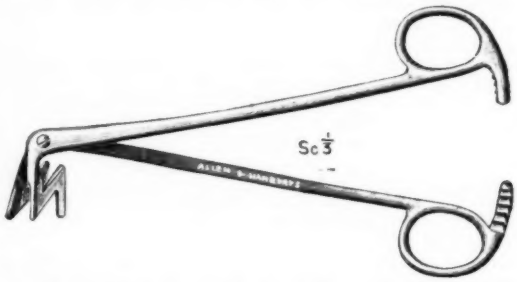
JOURNALS.

JOURNAL OF INDUSTRIAL HYGIENE.—Various aspects of the cost of illness to industry are considered in the issue for April. The first paper is by E. W. Phillips dealing with tuberculosis in an industrial group. Free medical service without special attention to prevention and detection of tuberculosis did not control the disease. The group of workers concerned were railroad employees, among whom the annual tuberculosis rate was about 1 case in 800. It costs on an average 4600 dollars to put an advanced patient in condition to resume work; a moderately advanced case costs about 1050 dollars, and an early case about 450 dollars. At the same time the mortality in the advanced cases, within four years of detection, was nearly 40 per cent.; while all the moderately advanced and early cases recovered and were able to return to work. The occurrence of nervous illness in industry is discussed by Millais Culpin, who points out that such industrial neuroses as cramp among telegraphists, which he has specially studied, and miners' nystagmus are really only particular manifestations of the existence of a large mass of nervous individuals. A paper by him on Nervous Disease and its Significance in Industry has appeared in THE LANCET (1928, ii., 897).—The third aspect is the relation between lead absorption and compensation, which is presented by M. R. Mayers. It is based on a physical examination of 381 lead workers. Of these, 149 were suspected of lead absorption, but when laboratory methods were applied in 39 cases no basis for the clinical diagnosis was found. On the other hand, among the 232 cases free from any clinical suggestion of lead absorption, laboratory research showed that in 112, or almost half, active lead absorption was taking place. The conclusion drawn is that when laboratory research supports clinical symptoms the case is undoubtedly one for compensation. When there are no clinical symptoms, even though laboratory research indicates lead absorption, there is no disability, and so no case for compensation. The doubtful cases are those where laboratory research shows no absorption, but where there is disability on clinical grounds ascribable to lead. Most of these cases probably are not associated with lead poisoning, hence compensation should not be awarded.

New Inventions.

PERITONEAL TETRA-TOWEL FORCEPS.

THE use of tetra cloths is now regarded as almost an essential in the technique of abdominal operations. The difficulty is suitable forceps. The forceps shown in the figure overcomes many difficulties. It lies flat under the tetra cloth as it has an abdominal curve. Its bite is also horizontal and dips vertically



into the wound over the skin edge. The fixation of the towel to the peritoneum is broad and does not damage or tear the peritoneum, and the instrument is sufficiently large to prevent possible loss in the abdomen. Two forceps on each side are required for the average wound—the proximal two are attached by the operator with the assistant holding the peritoneal edge and towel edge in apposition, and the distal two are controlled by the assistant. These instruments are of particular help in Cæsarean sections.

The forceps are made by Messrs. Allen and Hanburys, Limited, Wigmore-street, London, W.

W. MCK. H. MCCULLAGH, M.B., B.Ch. Belf., F.R.C.S. Eng.

ELECTRICALLY ILLUMINATED NASAL SPECULUM.

THE accompanying illustration shows a simple electrically illuminated nasal speculum. The light-carrier is of the Jackson type, set at an angle through the blade of the speculum, and can be removed for cleansing. The instrument is useful for bedside examination, when it is difficult to obtain a satisfactory light. The same principle could be applied to the Thudichum type of speculum.

The instrument is made by Messrs. Mayer and Phelps, Chiron House, New Cavendish-street, London, W.

JOHN E. G. MCGIBBON, M.B., B.S. Lond., D.L.O. Eng.

Radon in Cancer of the Œsophagus.—Mr. Musgrave Woodman calls attention to an inaccuracy in our report of his remarks at the Royal Society of Medicine (THE LANCET, June 15th, p. 1250). When speaking of the external approach to the œsophagus by the operation of thoracotomy, he mentioned that few patients would be suitable for this treatment, but in contrast to this, almost all patients were suitable for the simple operation of introduction of radon through the œsophagoscope.

THE LANCET.

LONDON: SATURDAY, JUNE 22, 1929.

THE MEDICAL PROFESSION IN THE NEW PARLIAMENT.

WHEN the last Parliament assembled early in 1925 we were able to publish the portraits of 12 members of the medical profession who had become members of the House of Commons. We are happy to do the same for the new Parliament which meets on Tuesday next when the profession will have 18 representatives, excluding those in the House of Lords. They belong to each of the political parties; they also, for the first time, include members of either sex. The change of Government has caused Major WALTER ELLIOT to lay down his responsibilities for Scottish affairs in an office which he has discharged with marked ability and enthusiasm and to the satisfaction even of his political opponents. But medicine has now a larger share of ministerial appointments than before; we congratulate Dr. DRUMMOND SHIELS on his advent to the India Office where his experience of the not dissimilar problems of Ceylon may be useful; and we welcome the return to office of Dr. ADDISON, the new Parliamentary Secretary to the Ministry of Agriculture.

The incoming Cabinet's programme of legislation will not be officially revealed until the KING'S Speech is read at the opening of Parliament. In the present balance of parties we can expect no major measures except by way of compromise and consent. Parliamentary time in July must be devoted to completing the year's financial arrangements, of which last session's Finance Act was only a brief instalment. Unemployment, foreign affairs, and the mining industry are likely to demand full discussion. The Ministry of Health will be busy with administrative changes due to the recent Local Government Act. Here our medical members will watch with special concern the effect upon institutional facilities and upon our existing system of voluntary hospitals. Shall we hear news at last of a new Factories Bill? This project, so often mentioned in previous King's Speeches, was the one admitted failure in the late Government's claim of pledges fulfilled. Undoubtedly the past five years have seen several useful measures, of particular interest to the medical profession, placed upon the statute-book either on the initiative or with the aid of medical members. The list includes the Public Health Act of 1925, the Therapeutic Substances Act, an important Mental Deficiency (Amendment) Act, attempts to mitigate the smoke nuisance and lead paint poisoning (though these efforts fell short of what many desired), the Coroners (Amendment) Act of 1926, and the improvement of the law of death registration linked therewith, provision for the registration of nursing homes, amendment and consolidation of the Food and Drugs Acts, and a re-statement of the poor-law which already demands a further revision. This output, in itself an indication of increasing popular interest in public health, was attained in a Parliament dominated by a docile and substantial majority such as may not be seen again for several years. These conditions of party government have made us forget the difficulty of legislating in the absence of such support. Private members' Bills may have better chances of success if both Houses of Parliament decide to pursue recent suggestions for carrying over a Bill from one session to another. A great opportunity occurs in the field of local legislation for progressive health measures, some of which—as in a recent Edinburgh Corporation Bill—raise acute problems of medical treatment. One topic on which Parliamentary action is long overdue is the control of patent remedies. A Select Committee examined the evidence thoroughly and reported in 1914, but nothing has been done since. Other topics which demand attention are rivers pollution and atmospheric pollution. Most important of all, perhaps, is lunacy reform. Parliament has ignored the views of expert advisers and too little is done to combat the early stages of mental disease or to provide treatment for the cases which fall short of certification. Nor must the fact be ignored that certification itself, the key to the present processes of institutional treatment, will break down if the certifying practitioner, upon whose evidence a judicial order is made, is to be exposed to litigation and to such huge awards of damages as have been recorded in recent years.

The medical M.P. is elected, we all know, to represent a constituency, not to press the sectional claims of a particular profession; but he does not divest himself of his special knowledge when he goes to Westminster, nor will his contributions to debate on technical or professional subjects, if delivered with reason and moderation, fail to command respect. Some of these subjects will be controversial. Health insurance, vaccination, vivisection, the position of the unregistered practitioner—here are instances of past controversies from which the medical M.P., whatever side he takes, could hardly stand aloof. Such instances will recur in plenty; if it be only to conciliate the army of new feminine voters, Parliament must give increasing attention to the health of the family and to public hygiene.

TRIAL LABOUR FOR THE SECOND CHILD.

A TRIAL labour is a labour experimentally allowed to proceed, though the obstetrician has reason to doubt whether a living child of normal size can be delivered at full term. The practice has arisen in recent years as an expression of the reaction which has followed the advocacy of induction before term or of Cæsarean section in all cases where grave disproportion between mother and child is suspected. The expectant attitude now adopted by many obstetricians must not, of course, be confused with the hearty optimism which moved practitioners of an older generation, when a patient came to book her confinement, to note in a diary the probable date, and to dismiss her with the cheerful assurance that all would be well. The essential feature of a trial labour is that it involves more anxious watching than any other method. It should never be conducted in the patient's home, but in an institution equipped and staffed for all emergencies. Its purpose is to save the individual patient from unnecessary interference, not only in her first but in subsequent labours.

Why are the devices for coping with disproportion, which were held up as triumphs of obstetric art not so long ago, being superseded in many clinics now by expectant tactics? Is it because serious drawbacks to these methods have lately become apparent or because experience has shown our criteria of measurement

or our means of estimating the forces in labour to be unreliable? The new teaching postulates that in doubtful cases—and a good many fall into this category—the patient should be admitted into an institution where her labour can take place under supervision but with no interference in the early stages. If no progress is being made after a period to be determined by the observer and, in respect to which no directions appear to be laid down to guide the less experienced, Cæsarean section is to be performed, since high forceps are now universally condemned. It is claimed that in practice the operation is often found to be unnecessary, because the moulding of the head is so great that a live child is often delivered naturally when this outcome seemed most unlikely. We need seek no further reason for an alteration in obstetric tactics. We have all of us heard of infants emerging per vias naturales, even while preparations were being made for a Cæsarean section, and of the birth of a healthy, large child to a mother whose earlier pregnancies were artificially terminated at the eighth month; but we have assumed that the previous examinations had been conducted by an inexperienced or timid obstetrician, or that the cases were exceptional. Evidently, however, obstetricians have good reason to believe that in a considerable proportion of cases in current practice a prognosis founded on measurements and estimates is too gloomy, though they are unable to state precisely and quantitatively what extra allowance should be made in any given circumstances. It is possible that observation of large numbers of women whose trial labours have been uneventful will give a standard of probabilities which will save their sisters from uncertainty.

Has the point of view of the individual patient been sufficiently considered by the protagonists of trial labour? It would be interesting to learn the views of the educated prospective mother whose pelvic measurements are not normal on the proposal to subject her to a trial labour of uncertain duration or discomfort, which may possibly end in an abdominal operation. If the issues were plainly put before her, she would probably far prefer an induction after the eighth month for her first child, though she might be willing to try experiments for her second should the induced labour show considerable margin. The obstetrician may claim that the conduct of a labour is his responsibility, which cannot be shared with the patient. But her coöperation must be enlisted, not only because her consent to a confinement in an institution must be obtained, but because on her fortitude and patience the issue will largely depend. The desirability of submitting to a test which, even if it fails, will give information guiding the conduct of future pregnancies, is not likely to be considered at a time when the mind is concentrated on hopes and plans for this first child. The emotions aroused can hardly be expressed in terms of stress and strain, but the woman is conscious that if her first child is lost or spoilt the shock and distress may have a profound effect on her subsequent life. This anxiety for the first child is not the prerogative of educated women, whose sisters in other classes differ from her not in emotion but in articulateness. It is a point worth considering whether induction should not be continued as a routine for primiparæ with contracted pelves, reserving the trial labour for the second pregnancy should there have been an encouraging margin when the first child was delivered. Even more useful information would thus be obtained, and the patients would be more likely to face the ordeal without dismay.

VACCINATION DANGERS.

HEADLINES in daily papers during the past week have contained such phrases as The Death Roll of Vaccination; A Number of Poison Deaths after Vaccination; and Sleepy Sickness Opens New Controversy, which have instilled fear into such newspaper readers as are still susceptible to suggestion of this kind. A Society leader has publicly announced her satisfaction that none of her seven babies has been vaccinated, and the responsible chairman of an Irish Board of Health, when called on to deal with vaccination defaulters, is reported to have said, "I would not advise that proceedings be instituted against them at present in view of the reports that are current about sleepy sickness as a result of vaccination." While parents are still obliged to have their children vaccinated against small-pox, the gap left by conscientious objection has become so wide that in the town of High Wycombe, for instance, exemption was claimed for 93 per cent. of babies born in the last year on record. Is it possible, one may well ask, for the still small voice of preventive medicine to make itself heard above the noise and turmoil of the jarring elements? Prevention is always at a disadvantage, for it is continuously destroying the object-lessons which render its teaching effective. The Anti-vaccination League says that small-pox in England has for many years been a less fatal disease than chicken-pox, and invites us to conclude from this that vaccination is futile. But we may equally well regard the facts as evidence of its success. Vaccination would certainly be futile if small-pox were not a potentially killing disease, but the Registrar-General's figures for the last quarter, which have been regularly quoted in our columns, are a reminder of what punishment severe small-pox when it is reintroduced inflicts on the unvaccinated.

What are the incidents which have given rise to these scare lines? One is recorded by Dr. JOHN TAYLOR, pathologist to St. George's Hospital, on another page of our present issue, where a healthy woman, 31 years of age, vaccinated on May 22nd, died on June 7th with post-mortem findings consistent, as Dr. TAYLOR writes, with those recorded in other cases of post-vaccinal encephalitis. Inquests have also been held in London on girls aged 10 and 14 years, in each of which death was regarded as due to encephalitis following primary vaccination. It was quite plain, as the Coroner for Westminster (Mr. INGLEBY ODDIE) pointed out in one of these cases, that there was nothing unsatisfactory in the lymph or in the method of vaccination or in the treatment of the arm. Whatever view may be taken by pathologists about the exact nature of the infecting agent, unhappily there is no reasonable doubt that these deaths must be regarded not only as post-vaccinal but to some extent as propter vaccinal. The main facts of this risk, as we now know it, were set out with care in a report by the Commission on Small-pox and Vaccination presented to the Health Organisation of the League of Nations at Geneva last August. The problem has arisen in consequence of the events of the last few years in the Netherlands and Great Britain. In the Netherlands 139 cases of disease of the central nervous system following vaccination were described during the period 1923–27, of which 41 were fatal; and in England and Wales during the two periods covered by the reports of the Andrewes (1922–23) and Rolleston (1926–27) Committees, 87 similar cases occurred, of which 48 were fatal. The period between vaccination and the onset of symptoms was usually between 9 and 13 days. In both countries a predi-

lection of the disease for children of school age was noted, only 8 of the English series of 87 being under two years of age. Most of the cases in both countries occurred in children whose vaccination, judging from all ordinary signs and cutaneous reactions, had run a normal course. The Geneva report suggested further inquiry into the existence of post-vaccinal encephalitis in countries other than the Netherlands and England as an essential preliminary to the proper understanding of the causes which have operated to produce this disease in these two countries. Our own Ministry of Health has asked to be kept informed of all cases of central nervous disease in which vaccination had been performed within four weeks of the onset. If, however, the fact of recent vaccination were made obligatory on the certifier, a retrospective investigation of fatal cases would still be possible. The Commission spoke of the minute risk of encephalitis in proportion to the vast numbers of normal vaccinations, a point emphasised in the Rolleston Report by the statement that 51 deaths were reported in a period during which approximately two million vaccinations and revaccinations were performed at the cost of the rates and more than three million charges of Government lymph were issued. Crucial indeed is the fact that disease of the central nervous system is a complication of the utmost rarity among infants vaccinated under the age of two years and of equal rarity after revaccination of older children or adults. In the Netherlands primary vaccination at school age was the rule, but the experience of 1923–27 was sufficient to shake official satisfaction with this method and to occasion a temporary suspension of the administrative measures on which vaccination at school age rested.

Infancy is a dangerous adventure but vaccination happily is not one of its major risks, and the inconvenience it produces might be mitigated. The Rolleston report made a suggestion, warmly endorsed by Mr. ODDIE at one of the recent inquests, in favour of limiting the number of vaccine insertions at each operation. It does not appear to have been determined on any adequate scale what is the smallest amount of virus sufficient to produce immunity, but the report regarded the probable loss of duration of individual immunity, being the result of substituting a single for multiple insertions, as fully compensated by the readier acceptance of vaccination. Dr. G. H. HART and other medical officers of health have long protested that it is a mistake to insist on four insertions, believing that the practical difficulty in obtaining consent to vaccination would largely disappear if the milder method were permitted. But public vaccinators, it seems, have not yet been given discretion in the matter as a sequel to this recommendation. The argument for infant vaccination has been immensely strengthened by the immunity it gives not only against small-pox but against the worst danger (rare though it is) of primary vaccination later. It may be that in the years immediately following on infancy encephalitis, if it should occur may take on a milder aspect. The interesting case recorded in our columns this week by Sir THOMAS HORDER gives some hope in this direction. A boy, 4½ years old, who became drowsy on the eighth day after a primary vaccination and was stuporous on the eleventh, recovered rapidly after intrathecal injection of 5 c.cm. of the serum of his mother who was vaccinated on the same day as the child. This child, who was suffering from a febrile disorder of four days' duration at the time of vaccination, received four insertions of vaccine, and Sir THOMAS remarks that whether the Committee's recommendation of one insertion only during infancy (with revaccination at 5–7 years and at 14–16 years) be followed or not, it should certainly be followed in all children who are suspected of recent infections of whatever kind. The position of small-pox vaccination is unique. As the sole established instance of the use of a living virus as an immunising agent it presents difficulties. We have much sympathy with Mr. ODDIE'S view that the recommendations of the Rolleston Report should receive the attention they merit.

Annotations.

"Ne quid nimis."

RIVERS POLLUTION.

LAST month's conference on the pollution of streams and rivers by town sewage and trade refuse did something to press upon public attention a subject too easily forgotten. Just as it is lamentable that, while one Government department is interested in smoke abatement and a purer atmosphere, another department sanctions the establishment of a fresh source of pollution in the Battersea power-station, so it is lamentable that some of our administrators should have imported a great continental industry like sugar-beet cultivation without forethought of the effect of the trade wastes from sugar-beet factories upon streams of which others of our administrators are concerned to secure the purity. A fresh threat to rivers where salmon still abound is to be noticed especially in the County of Devon. The multiplication of garages, usually swilled out every morning, sends oil in ever greater quantities into public sewers or storm-water drains; if it does not actually destroy the fish in the rivers, or drive them back to the sea, it spoils the gravel banks and sedges where the immature fish find their food. On the bigger issues other questions arise. Are we devoting enough time and money to research? Are we solving the problems of particular trade effluents, trade by trade? Cannot more be done to fix standards and enforce them? Can we not make up our minds what is the duty of the local authority in respect of providing means of disposal, and whether the trader is or is not to have a right to discharge his waste into public sewers? To turn a topic over to examination by a Royal Commission is notoriously a process of postponing action. Almost a generation ago the Royal Commission on Sewage Disposal made its recommendations, yet little or nothing has beeen done. Some say the law is sufficient if it were only administered effectively; others say the law is useless in itself. Several instances of expensive and protracted litigation have probably discouraged local authorities from further effort. When the Joint Advisory Committee on Rivers Pollution had reported, the Ministry of Health urged the formation of Joint Watershed Committees. Is it because of jealousies among the local authorities or because of other preoccupations at the centre that results are so slender? Should the central authority be armed with fuller powers to give final decisions without reference to the law-courts, and should that central authority be the Ministry of Health or some other body old or new? The public knows that the state of its rivers is getting steadily worse, though pollution seems to be successfully combated in particular cases. In spite of the necessity of not hampering commercial undertakings, the public wants its rivers clean. If the demand is not yet very loud, it will grow louder, for there is increasing interest in the preservation of the country's amenities. When the demand is loud enough, something will have to be done. The task will be easier if tackled now.

COMPARATIVE ANATOMY OF THE CEREBELLUM.

THE Herter Lectures at the Johns Hopkins Medical School were given last winter by Dr. Iven Ingvar[1] of the University of Lund in Sweden. The first was entitled the Phylogenetic Continuity of the Central Nervous System, the second was devoted to a discussion of the function of the cerebellum, and the third dealt with the pathological changes underlying the phenomenon of the Argyll Robertson pupil. The chief interest undoubtedly centres in the first lecture. Phylogenetic continuity is an established principle of anatomy, but while the discovery of homologies in different species is often regarded as an end in itself, the principle is capable of being used as a means of elucidating obscurities in human anatomy, and Dr. Ingvar has thus used it in an endeavour to discover the primary anatomical divisions in some difficult parts of the central nervous system, particularly in the cerebellum and in the thalamus.

His comparative studies of the cerebellum were already well known to neurologists. In the human cerebellum the old anatomists found various divisions to which, without any knowledge of their significance or relative importance, they gave fanciful and picturesque names—vermis, pyramis, tonsilla, nidus avis, and so on—with which our memories are still burdened. Yet these names were for centuries only veils to cover ignorance and hampered rather than assisted the understanding of the organ's nature and function. In the nineties of last century the embryological studies of various English workers—Stroud, Bradley, Elliot Smith—brought a new knowledge of cerebellar anatomy, and with Bolk's comparative studies yet another advance was made. Bolk's merit is that he revealed in the cerebellum throughout the mammalian class a constant morphological system; he taught that in all mammals it was formed on the same uniform principles. In all mammals the deepest of the transverse fissures of the cerebellum is the "primary sulcus"—the sulcus which is the first to appear during embryological development, the mass in front of this sulcus Bolk called simply the anterior lobe and all that developed caudal to it he called posterior lobe. The anterior lobe is subdivided in all mammals into four lobules. The posterior lobe presents more difficulty; its rostral (or anterior) portion has the same plain pattern as the anterior lobe and Bolk called it the lobulus simplex. Behind the lobulus simplex two sagittal fissures divide the main mass of the posterior lobe into a medium portion (the inferior vermis), which Bolk called the lobulus medianus, and two lateral portions, the lobuli laterales (the cerebellar hemispheres of the old terminology). Ingvar has endeavoured to carry Bolk's work a stage further. Surveying the cerebellum throughout the vertebrate phylum he concluded that another sulcus separating off the most posterior part of the vermis, with its attached flocculi, was an elemental one. He consequently gave the name posterior lobe to the portion separated off by it, and the structures between it and the primary fissure he called the middle lobe. We may observe that Elliot Smith, from a study of the embryology of the cerebellum, had made a similar division nearly twenty years earlier. Ingvar's division, whilst nearly identical with Elliot Smith's, assigns the pyramis to the posterior lobe, whereas Elliot Smith's assigns it to the middle lobe; when we consider the difficulty of deciding among the neighbouring fissures which corresponds to a particular one in other animals, we may find guidance in the connexions between adjacent parts; the pyramis is connected on each side with the lobulus biventer (digastric lobe) which both authorities assign to the middle lobe, and if this connexion is at all intimate it seems probable that the pyramis also belongs to the middle lobe. That, however, is a relatively small matter and on the main lines there is substantial agreement. Supporting evidence for the division of the cerebellum in this way is afforded by the fact that the fibres which enter it are distributed according to the lobes thus described—those from the spinal cord to the anterior and posterior lobes, those from the pons to the middle lobe, and those from the labyrinth to the posterior.

Encouraged by the evident services of phylogeny to the study of the cerebellum, Ingvar went on to examine by the same methods the manner of division of the thalamus. Again giving his attention largely to the brains of birds, he recognised in them all the thalamic nuclei of mammals, the greatest difference between the two classes being the much stronger development of the lateral thalamic region in mammals. The most conspicuous formation in the avian thalamus is the nucleus rotundus and this in Ingvar's view corresponds to the nucleus ventralis of the mammalian thalamus, the homology, he finds, is again supported by the similar fibre connexions of the parts. That there should be such correspondence in the structure of the thalamus in the two classes and yet such enormous difference in the development of the cerebral hemispheres suggests that the thalamus is largely independent of the cerebral cortex and that its nuclei are laid down and developed without regard to cortical formations. The lecture concludes with a few paragraphs on phylogenetic continuity as seen in the cerebral hemispheres, but these are not based on Dr. Ingvar's own work and he scarcely develops the subject. Such a method of anatomical study is a fascinating one, and if it is rigidly controlled by every available means it is certainly likely to yield valuable results.

[1] Bulletin of the Johns Hopkins Hospital, vol. xlii., No. 6, December, 1928.

ICTERUS NEONATORUM.

THE pathology of jaundice occurring in the newly-born has been subjected to close study in recent years and its classification has been greatly improved. When syphilis, sepsis, and excessive fragility of the red blood corpuscles have been excluded, three ætiological possibilities remain to be considered. The case may be an example of "physiological icterus"; it may belong to one of the more severe familial forms, such as icterus gravis neonatorum; or, finally, the so-called congenital obliteration of the bile-ducts may be responsible. In the last-named group it has been well known for many years that a cirrhosis of the liver is also present, and Sir Humphry Rolleston is inclined to regard this as the initial lesion with obliteration of the extrahepatic ducts as a subsequent development. Following this teaching several cases have been reported in which congenital obliteration of the bile-ducts was diagnosed on the micropathology of the liver, though the extrahepatic ducts were quite patent. The condition known as physiological icterus neonatorum which occurs in about half the infant population has been attributed to the destruction of the excessive number of red blood corpuscles with which every infant is born. The difficulty of accepting this view has been the fact that every infant does not suffer from jaundice. Lately an attempt has been made to elucidate the condition by comparing the blood groups of the mothers and infants, and in a recent paper[1] Dr. G. Lenant and Dr. S. Biró enlarge on this question and also on the occurrence of isoagglutination phenomena in the blood of the newly-born. As far as a study of 100 cases by these authors will permit of generalisation, it seems to be established that severe icterus neonatorum is twice as likely to be present where agglutination between the mother's and the child's blood occurs as when this is not present. In another communication[2] to the same journal, Prof. C. de Lange, with the coöperation of Dr. A. K. W. Arntzenius, gives a very interesting account of

[1] Jahrbuch f. Kinderheilk., May, 1929, p. 77.
[2] Ibid., p. 1.

familial "icterus gravis neonatorum," or as it is here called "icterus familiaris gravior." In these cases several children in the same family are born with an intense jaundice and usually survive only for a few days. Those who survive longer often develop curious nervous symptoms consisting of head retraction, spasticity of the limbs, and sometimes tonic contraction of the upper extremities. At autopsy there is no evidence of any fibrosis in the liver, and very little of degenerative or other changes in the liver cells. Most of the organs are deeply bile-stained, but in the brain there is especially deep staining of the basal nuclei. The blood picture shows signs both of gross destruction of blood and of regeneration. Three theories have been advanced to account for this rare condition—it might represent a disease of the blood-forming apparatus of the child, it might result from toxins acting in utero and arising either from the mother or from the fœtus itself, or it might be due to hæmolysis of the child's blood caused by the interaction of agglutinins and isoagglutinins. Some support is lent to the toxin theory by a case of severe congenital œdema, "hydrops universalis fœtus," described by Prof. de Lange. The mother was very œdematous with albuminuria, and corresponded to the "toxæmia of pregnancy" type of case. The blood picture of the infant and the section of liver obtained at autopsy were exactly similar to those seen in the cases of icterus gravis, and, moreover, a connecting link is found in reports from the literature of children born in a condition of generalised œdema to mothers whose previous infants had fatal icterus. This sequence suggests that icterus gravis neonatorum is due to some toxin transmitted from mother to child. Dr. W. Scholtz [3] reports a family in which the two first children were slightly jaundiced at birth; in each the jaundice became intensified on the fourth day and both infants died a few days after. On the assumption that the intensification of the jaundice on the day after the secretion of milk started was more than a coincidence, two children born later to the same parents were artificially fed. These showed only a mild transient jaundice and progressed favourably. A family history of asthma and of intermarriage was noted. Unfortunately the cutaneous reaction of the surviving children to the mother's milk was not tested. The obscurity surrounding various types of congenital jaundice is lifting; if further study of the new views leads to their confirmation, light may be thrown on the pathology of certain other congenital abnormalities.

NICOTINE IN CIGARETTES.

THE practitioner is handicapped in forming an opinion of the clinical effects of smoking by the lack of scientific data concerning the actual toxicity of tobacco in the various forms in which it is taken. Some useful work has lately been done by Dr. A. Winterstein and Dr. Ernst Aronson, of the Department of Agricultural and Physiological Chemistry at the Technical High School of Zürich, on the actual and effective nicotine content of various kinds of cigarettes.[4] They point out that previous estimates have been compromised by the absence of a satisfactory method of measuring nicotine, but that Fühner's method gives readings of great accuracy; he estimates with a cymograph the muscular contractions of a leech under the influence of nicotine. They found that the toxicity of a cigarette is determined not only by its nicotine content but also by the variety of its tobacco, and its humidity, shape, and density. Those who inhale absorb three times as much of the poison as those who do not. Short, thick cigarettes produce twice as much nicotine as long and slender ones, and loosely rolled cigarettes 30 per cent. more than those which are rolled tightly. The nicotine given off by damp cigarettes is 30 per cent. less than that produced by dry ones. The quantity of nicotine which reaches the mouth therefore depends on the resistance offered to the smoke in its passage through the tobacco; if this resistance is low the amount passed will be high. Dark and strong tobacco yields more than light. An important feature of the investigation was the discovery that "hygienic" or "denicotinised" cigarettes contain just as much of the alkaloid as ordinary ones, and that a cotton-wool filter does not diminish the quantity in the smoke. It was found impossible to reduce the output of nicotine by chemical means. The authors suggests that legislation should be passed to restrict the use of the term "nicotine-free" or "low nicotine" to tobacco containing not more than 0·8 per cent., which would deliver at the mouth not more than 0·4 mg. of nicotine per gramme of leaf. They point out that so far it has not been possible to produce a tobacco with this low content that has an acceptable aroma, but that selective cultivation should solve the difficulty. It is, they say, a fact that certain tobaccos contain only one-third to one-seventh of the quantity of nicotine present in a high-nicotine brand, and they hope that propaganda will encourage a demand which will make the necessary research worth while. They make no mention of other toxic bases in cigarettes, such as pyridine, and presumably their method of measurement gives the mass result of all the toxic constituents. Nevertheless their tables, which are very full, will provide valuable information for those interested in this question.

TREATMENT OF PULMONARY TUBERCULOSIS WITH SANOCRYSIN.

IN November, 1923, before Prof. Möllgaard had published his investigations into the effects of sanocrysin on tuberculous animals, Dr. K. Secher began to test this drug in human beings. Since then he has continued to study its effects in man, and his latest publication, in *Nordisk Medisinsk Tidsskrift* for June 1st, includes a summary of the results achieved in the 322 patients hitherto treated. He classifies them in three groups, according as they (1) became well, (2) became better, or (3) showed no change or became worse. Among the 191 patients in the first group, there were 53 whose disease was slight, as many as 45 of these 53 being sputum-negative. There were also 41 whose disease was severe, but even among these cases there were as many as 19 sputum-negative patients. In the same group were 70 cases of pleurisy, 14 of glandular tuberculosis, and 13 of tuberculosis in children under the age of 15. In the second group, which contained 68 cases, there were 55 in which the disease was severe, 47 of these 55 being sputum-positive. There were also 6 cases of very severe disease, 3 of pleurisy, and 4 of tuberculosis in children under the age of 15. In the third group, which contained 63 cases, every case was classified as one of very severe disease. Dr. Secher has come to the conclusion that this class of case is unsuited for chemotherapy. In several of these cases the treatment was attempted as a therapeutic essay or as a consolatary expedient. "This group," he says, "can be entirely eliminated in the future." An unsatisfactory feature of Dr. Secher's material is the lack of controls. Of his 73 patients suffering from pleurisy, 70 were cured, and three became better—a happy sequel, the significance of which must, however, be judged in the light of the fact that the overwhelming majority of such patients get well and keep well with nothing more specific in their treatment than prolonged rest and fresh air. The same criticism is applicable to the 53 sputum-negative patients whose disease was slight, and whose recovery, it is implied, was connected with their treatment with sanocrysin. More convincing than Dr. Secher's statistics are his records of isolated cases, and no doubt his continued advocacy of this treatment depends

[3] Jour. Med. Assoc. of South Africa (B.M.A.), May 11th, p. 252.

[4] Schweiz. Med. Woch., May 25th, 1929, p. 550.

chiefly on his clinical evaluation of a large number of individual cases. His discussion of the dosage resolves itself into a criticism of the timid procedure which is "a tuberculin therapy and has nothing to do with sanocrysin treatment," and of a rule-of-thumb schematic procedure. He recommends the most cautious individualising, the graduation of the dosage according to the patient's weight, the character and extent of the disease, and the nature of the reaction following the previous injection. He usually begins with a dose of 0·5 g.—i.e., approximately 0·01 g. per kg. of body-weight. At the second and third injections, 0·75 g., or 1·0 g., is the usual dose. The intervals between these three first injections are usually two clear days, the later intervals being from five to six days or even longer if the reactions point this way. The injections are continued until what Dr. Secher calls "effective doses" no longer provoke a reaction. The usual number of injections is five or six, but he sometimes gives up to ten, the average dose—"a really effective dose"—in one series of cases being 0·0167 g. per kg. body-weight. Dr. Secher's review of the results achieved by various clinicians suggests very explicitly that pessimism may be correlated with timidity of dosage, the curve illustrating the transition from pessimism to optimistic confidence in sanocrysin running parallel with the rising curve of the dosage.

SCARLET FEVER CARRIERS.

SEVERAL outbreaks of scarlet fever ascribed to carriers have recently been described by Dr. Ruth Tunnicliff and Dr. T. T. Crooks.[1] In the first epidemic the infection was introduced into the ward of a children's hospital by a boy who was admitted apparently during the incubation stage of the disease for he developed scarlet fever three days afterwards. Another case was noted on the same day and still another nine days later. The usual measures were enforced with regard to quarantine but further cases nevertheless appeared in the same ward on the twelfth and thirteenth days after the last case. Throat cultures were now taken from everyone in the ward, including doctors, nurses, and wardmaids, and hæmolytic streptococci, said to be specific for scarlet fever, were isolated in almost pure culture from a doctor and a nurse who had had a sore throat about a fortnight before. Further examination showed that at the end of five days the streptococci had disappeared from the throat of the doctor, but the subsequent history of the nurse is noteworthy. She was allowed to remain on duty in the same ward and about a month later three new cases developed among the patients, although face masks were now being worn by the nursing staff. On the occurrence of these cases she was still found to be harbouring a hæmolytic streptococcus and was taken off duty from the ward and given work which only permitted contact with other nurses. At the end of about another month a colleague who had been in the habit of visiting her room developed scarlet fever, and at this stage her throat was examined by an ear and throat specialist. Chronic tonsillitis was found and the specific streptococci were isolated from the tonsils when they were removed. After operation throat cultures failed to reveal the presence of hæmolytic streptococci and no more cases of scarlet fever appeared in the ward. Tunnicliff and Crooks's paper also gives details of two family outbreaks of scarlet fever in which the only possible contact of the children with the outside world was by means of the father, who was in each case found to be harbouring a hæmolytic streptococcus of the type specific for scarlet fever. Their whole argument clearly rests on their claim to be able to distinguish this specific strain, for this is the basis of proof that the persons described as carriers were accurately so determined. Epidemiological evidence is overwhelming in favour of carriers, both healthy and convalescent, being responsible for the spread of scarlet fever, and since the streptococcal ætiology of scarlet fever was established the epidemiological indications have fitted in very accurately with what we know of the distribution and habitat of the hæmolytic streptococcus. Absolute proof awaits better classification of the streptococci, but in this connexion it may be noted that Miss Tunnicliff[2] has previously described a method using the opsonic technique for differentiating the scarlatinal streptococcus. It does not seem difficult to carry out and she says that it is as quick and accurate as the cultural diagnosis of diphtheria. If this work can be confirmed it will go far to simplify the diagnosis of the disease and the determination of carriers, and will thus give good ground for administrative action which is at present based largely on strong suspicion.

[1] Jour. Amer. Med. Assoc., May 4th, p. 1498.

COLLOIDS IN MEDICINE.

THAT branch of science which is concerned with the properties and behaviour of colloids originated in biological investigation and many of its most notable advances have been made by those engaged in such work. This is not surprising if we consider how great a part is played in the life of animal and vegetable organisms by systems which are essentially colloidal. On the one hand, the microscope reveals the intricate organisation of the tissues, and on the other, chemical and biochemical studies show the complexity of the continuous changes in them. These changes, often bound up with the microscopical structure, are nearly all incompletely understood, and at present it is seldom possible to reproduce them independently of life. This is particularly true in the vast field of enzyme action, which is held to account for many of the vital processes, and seems to be much more complex than even the most intricate example of inorganic catalysis. Despite a wealth of brilliant research into its nature, the great problem remains unsolved—namely, the way in which the various groups of enzymes act so specifically, each promoting only one type of chemical change or synthesis and each attacking only a certain (often highly specialised) type of chemical compound, leaving unchanged other substances which may be almost identical chemically. New evidence has accumulated of late; comparison with organic catalysis has yielded many suggestive analogies; but the problem is so intimately connected with the peculiar properties of various groups of colloids that it seems clear that advance in the knowledge of enzyme action must go hand in hand with the advance of colloid chemistry.

The theory of enzyme action, though exceedingly important, is only one aspect, however, of the biochemistry of colloids. The ubiquity of colloidal phenomena in the body is indeed remarkable. It would, of course, be absurd to assign to colloids the position of being the sole factors of life, but they are nevertheless concerned, more or less, in every manifestation of life. In a recent book[3] some of the applications of colloids to biology and medicine are reviewed by a number of biologists, chemists, physicists, and bacteriologists who have for the most part made a special study of colloids as applied to some branch of medicine or of its allied sciences. Biology and medicine, and botany also, are fundamentally concerned with cell behaviour, involving the study of the "permeability of the membrane" and the properties of protoplasm. A great number of investigations bearing upon these questions have been made, outstanding observations beginning with those of Pfeffer and De Vries and their original concept of the osmotic nature of the living cell. Some of the difficulties of this concept were known to its authors, for by producing precipitation of tannin in certain cells by diffusion into them of

[2] Ibid., 1926, lxxxvii., 625.

[3] Colloid Chemistry: theoretical and applied. By selected International contributors. Collected and edited by Jerome Alexander. Vol. II. Biology and Medicine. New York: Chemical Catalog Company. Pp. 1029. $15.15.

various substances they showed the untenability of the simple concept of the cells as a small sac of fluid enclosed by a semi-permeable membrane, impermeable to all dissolved substances but permeable to water. Indeed it was soon clear that the original view of the strict osmotic construction of the cell would have to be abandoned, for on this view the cell could not take up food or rid itself of its excretory products. As an alternative it was often suggested that the term "semi-permeable" must be allowed a more flexible meaning, and must be supposed to be "permeable" to the things necessary to life or permeable only in one direction. As Martin Fischer remarks in the book to which we have referred: "A living cell is, however, capable of taking up and giving off water and of taking up and giving off dissolved substances and these two things may occur at different times or at one and the same time, and with the solvent and dissolved substances moving in the same direction or in opposite directions." To explain these phenomena is by no means easy even to-day. Many of the theories proposed are based on the idea that "imbibition" might play some part in the process. Fischer, who has thrown much light on water absorption by living cells under physiological and pathological conditions (œdema), thinks that there are two main factors quite distinct from osmosis—namely, the reaction of the fluid and its salt concentration, taking into account the nature of the particular salt involved. The exchange of water is largely reversible, and urea, pyridine, amines, and certain other substances increase the hydration capacity in a way quite distinct from the action of acids and alkalis.

These few examples show that the facts are being accumulated, though very slowly. There are theories to explain some of the facts but none to explain them all. Undoubtedly the slowness of advance since the days of Pfeffer is due to the need for a new science in the form of colloid chemistry, and this is now being developed to explain the phenomena.

THE TREATMENT OF POLYCYTHÆMIA.

NOT long ago Dr. W. Mackay drew attention in our columns[1] to the uses of phenylhydrazine in reducing the red cells of the blood in polycythæmia. In both his cases nothing but good came of the treatment, but toxic effects have been from time to time reported by other observers. In this country cases of polycythæmia are so rare as to make it hard for any one person to gain enough experience to lay down rules about dosage and general management. In America the diagnosis seems to be made more often, either because the disease is commoner or because diagnosis is more lax. The fact that certain cases have been recorded with red cell counts of only just over 5 millions favours the latter alternative, but in any case phenylhydrazine has been used on the human subject a good deal more frequently in America than in this country. As a result of their own experience and that of others Dr. H. Z. Giffin and Dr. H. M. Conner,[2] of Rochester, Minnesota, have laid down certain general principles to be followed in giving this drug. They point out that a very common cause of disaster after its administration is thrombosis, either of the mesenteric vessels or elsewhere, and on this account they lay stress on the importance of doing everything to prevent stagnation of the circulating blood. To this end the treatment is preferably ambulatory; if in hospital the patients should be kept out of bed as much as possible, or if this cannot be done, they should be given massage and passive movement. For the same reason the treatment should be used with caution in patients showing signs of advanced arterio-sclerosis. They consider that large doses are unnecessary and suggest an initial dose of 0·1 g. three times daily. This may be continued until from 1·5 to 3·5 g. have been taken according to the degree of blood destruction. Thereafter the drug should be given in short courses at intervals determined by the rate of red cell production. It is stated that patients soon learn the dosage which suits them and are able to judge for themselves when further courses are necessary. The treatment has its dangers, but has until lately offered almost the only satisfactory method of combating a disabling and dangerous condition. The newly introduced treatment by spleen extract promises to be less dangerous, but it remains to be seen whether it is equally effective.

[1] THE LANCET, April 13th, 1929, p. 762.
[2] Jour. Amer. Med. Assoc., May 4th, 1929.

RENAL STONES.

IN submitting a detailed analysis of cases of renal and ureteric calculus, Mr. A. R. Thomson[1] says that when he was appointed chief of the genito-urinary department of Guy's Hospital in 1910 he decided not to publish results until the department had been in existence for some time. As a basis for his report he has collected the post-mortem records at Guy's from the year 1890–1909, inclusive, and in order that "a curb might be placed upon any unfair opinions gathered from the records of one hospital," he has read through the case-sheets of nearly 13,000 cases treated at the Victoria Hospital for Children and at the London Hospital. His investigation has, therefore, been extremely thorough and his conclusions may be accepted with complete confidence. Among them are the following: (1) The incidence of stone is about equal in the two sexes, but in elderly people more males are affected than females. (2) There is a slightly greater number of stones on the right side than on the left. (3) The large number of bilateral stone formations, which is about one-third of the total number of cases, points to the seriousness of this condition. (4) Bright's disease is not uncommonly diagnosed when there is a renal or ureteric stone present, and a stone is often the cause of Bright's disease. Bright's disease following on stone formation is more common in males than in females, but bad kidneys, such as bilateral pyonephrosis, are more common in females than in males. (5) Stone may form in the urinary tract as a result of some wasting disease. (6) The commonest place for a stone to be found is the pelvis of the kidney. (7) Compensatory hypertrophy of one kidney, when the other is diseased, is not nearly so common as is generally supposed. (8) Stones may recur after operations for their removal, but this, Mr. Thomson thinks, may be due to carelessness on the part of the operator.

VACCINE THERAPY IN AMERICA.

IT is a little unfortunate that the one word "vaccine" should be employed in different senses. It was applied to the great and established discovery of Jenner in the prevention of small-pox; it was used to denote Wright's contribution to the prophylaxis of typhoid and allied infections; and it is used in relation to the treatment of infections by dead organisms. These three clinical methods do not stand on the same footing, but they have all given rise to extravagant claims at one time or another. The treatment of infections with vaccines, which is still in the experimental stage, is particularly open to abuse at the present time because so many conditions of unknown origin are put down to focal sepsis. When we hear of a case of soft corn of the foot treated with a streptothrix vaccine, and a case of lymphadenoma treated with a polyvalent fæcal vaccine, we feel that the patient is entitled to know that his medical adviser is putting his money on an outside chance, to say the least of it.

The question arises how far clinicians do, in fact, make use of vaccines is one to which no answer can be given in this country, although the price-lists

[1] Guy's Hospital Reports, April, 1929.

of commercial firms show that there is a constant demand. In the United States, however, Hektoen and Irons[1] have taken the trouble to write to over three thousand medical men in the hope of finding out. Their report is surprising, for the percentage employing vaccines, usually less than five, does not exceed 25 in any of the four groups into which the respondents are divided, and in furunculosis alone is that figure reached. The replies show almost complete unanimity in refusal to use *Bacillus coli* vaccines; only 0·25 per cent. treat colitis with vaccines, and no one employs them for tuberculosis or epilepsy. Hektoen and Irons point out that from 1906, when Wright introduced his vaccine treatment, to 1912, there was a large output of papers on the subject. Since then the papers have been fewer and apparently the method has fallen into disfavour. In the latest edition of Kolle and Wassermann's handbook, although much is written on it, significantly little is claimed. On the whole, however, it seems to be in greater disrepute in America than in this country or in Germany where questions are not uncommonly set in qualifying examinations on the "proved" values and methods of vaccine therapy. "Non-specific" or "shock" therapy is not considered in Hektoen and Irons's report, but the country in which Petersen has worked may be said to be the originator of this method, and we may suppose that it is widespread there. The use of such preparations here is undoubtedly spreading, and Ledingham has expressed the opinion that, where vaccines in treatment are efficacious, the result is due to non-specific reactions. Few would deny that, in staphylococcal skin infections, vaccines are often of value, but preparations of manganese give very similar results.

The exaggerated statements often made on behalf of vaccine therapy make this questionaire of interest, but it is unlikely that such an investigation will be made in England, and, after all, what the American doctor does is no more evidence of scientific fact than what the soldier said. It is, however, a straw showing which way the wind is blowing in the United States, and there are those who hold that a wind from the same quarter would not be disadvantageous over here.

MATERNAL MORTALITY.

Dame Janet Campbell, who has accepted an invitation to go out to Australia to give the benefit of her experience to the Commonwealth Government, was entertained on June 17th by the President and Committee of the United Empire Circle. Replying to Viscountess Elibank, who spoke of the widespread appreciation of her services, and expressed a hope that her mission would bring lasting help to Australia, she pointed out that maternity and child welfare was not a new subject in that country, and said she hoped to gain more from her visit than she expected to be able to give. In Australia, as in this country, maternal mortality was one of the most pressing problems, and it was a complex problem which could not be solved by any single line of approach, but only by the united action of all interested. A great deal of educational work was needed among the mothers themselves, and also among medical students and midwives, to equip them to meet the difficulties they might have to face. It should always be possible to summon the help of a consultant in time of need, for many maternal deaths would be avoided if the mother could have skilled attention at the right moment. Increased education and coördination would tend to bring about a reduction in the death and damage-rates among mothers, and also in the early infant mortality-rate associated with childbirth. Children between the ages of 1 and 5 years were at present somewhat neglected because no official body was responsible for them, and we must consider how best to watch over those children so that they might arrive at school age in a healthy condition. In the course of subsequent speeches the Countess of Birkenhead said that at the General Lying-in Hospital in the last ten years 26,198 confinements had been attended in the hospital and on district, the maternal mortality-rate being 1·6 per 1000; and Viscountess Erleigh paid a testimony to the invariably wise and far-seeing advice which Dame Janet had given in regard to plans for day nurseries.

[1] Hektoen, L., and Irons, E. E.: Jour. Amer. Med. Assoc., March 16th, 1929, p. 864.

CHEMISTRY IN CZECHO-SLOVAKIA.

Bohuslav Brauner has for many years been known by name to chemists as a professor at the Bohemian University of Prague, as well as an authority on atomic weights and general chemistry. It is, therefore, with interest that we welcome as fruits of his labours the appearance of an early number of the first annual collection of Czecho-Slovak chemical communications, published under the patronage of the Regia Societas Scientiarum Bohemica. The number contains eight papers by workers at the Charles University and the Polytechnic at Prague and at other similar institutions. Written in French or English, they include records of sound work in inorganic, physical, organic, and analytical chemistry. Not only the papers themselves but even the advertisement columns afford evidence of the intense desire of a country recently made autonomous to tell the world in languages better known than Czech that it is taking its place among the learned nations.

A MEDICAL "TALKIE."

Mr. Swift Joly will preside at the last meeting, for the present session, of the Section of Urology of the Royal Society of Medicine, to be held on Thursday, June 27th, when Sir John Thomson-Walker will give a cinematograph demonstration showing a "talkie" film. This is a demonstration by way of experiment, but we may have here the beginning of an important development in teaching. We understand that the film showing the operation will explain itself audibly as the operation proceeds, but that this does not imply that it will be a "close up" of the operator. The innovation is sure to attract a large audience.

THE Cavendish Lecture of the West London Medico-Chirurgical Society will be delivered at 8.15 P.M. to-day, Friday, June 21st, at the Kensington Town Hall, by Prof. Cl. Regaud, of the Radium Institute, Paris, his subject being Progress and Limitation in the Cure of Malignant Disease by Radium. A reception will be held from 7.30 P.M. onwards, and at 8 P.M. the Society's triennial gold medal will be presented to Sir Ronald Ross, F.R.S.

THE University of New Brunswick has conferred the honorary degree of Doctor of Laws upon Sir Charters Symonds, consulting surgeon to Guy's Hospital, who was born at Saint John. Sir Charters, who was prevented from attending the Encænial proceedings, signalised the occasion by founding a prize to be known as the James Symonds prize in history in honour of the original English settler at the mouth of the Saint John River.

NATIONAL CAMPAIGN AGAINST RHEUMATIC DISEASES. At a conference held in London last November an executive committee was appointed to draw up a constitution for a national campaign against rheumatism. This executive committee, of which Sir Thomas Horder is chairman, invites members of the medical profession to attend a meeting to be held at the house of the Royal Society of Medicine, 1, Wimpole-street, London, W., on Wednesday, June 26th, at 5 P.M., when a report on policy and constitution of the campaign will be received and a council will be elected. The hon. secretary of the committee is Dr. M. B. Ray, 6, Bentinck-street, W. 1.

The Clinical Interpretation of Aids to Diagnosis.

A Series of Special Articles contributed by Invitation.

XXXIV.

THE INTERPRETATION OF MENTAL TESTS.

I.*—Preliminary Considerations.

Probably very few of the problems of diagnosis and prognosis presented to the busy practitioner fill him with so profound a sense of his own limitations as that which faces him when he is asked by an anxious parent to give an opinion upon the mentality and the future prospects of a child or a young adolescent. General medical education, which provides the student with some knowledge, more or less vague, of the idiot and the imbecile, which he groups in his mind confusedly and erroneously with the insane, has omitted to inform him to any degree regarding the much larger class of the feeble-minded. In his general work after graduation he has but occasional opportunities of becoming acquainted with the type, in contrast to the children's specialist and the school medical officer, and as the feeble-minded generally do not present so marked physical traits as the idiot and the imbecile, he may be tempted to express favourable opinions regarding children who, before many years have passed, will demonstrate by their failures how uninformed the medical opinion had been.

At the outset the practitioner should beware of the temptation to utter comforting platitudes about "late development." One does not deny that late development occurs, but in the writer's experience it is extremely rare, and when there is a clear history of lateness in teething, sitting up, walking, talking, control of bladder and bowel, together with obvious signs of a mentality from 2 to 3 years below the normal for the child's age—we are assuming a child of about 7—it is safe to anticipate that there is a permanent lateness, becoming later every year, a permanent subnormality, that is to say, with all that it implies.

One of the practitioner's difficulties is that in these cases, as in the insane, he has almost entirely to abandon the search for physical signs which are his sheet-anchor in his routine daily work. There are, of course, a few definite types of deficiency which can be diagnosed by physical signs—the microcephalic, the hydrocephalic, the mongol, and the cretin being the chief of these. Their physical description does not concern us here, and in any case prognosis regarding their mental possibilities need give but little difficulty. The microcephalic rarely rises above the level of the low-grade feeble-minded. The mongol is always an imbecile, but mongoloid types exist with less marked physical features, who may rise a little higher. He is not always the last child of a mother exhausted by numerous pregnancies of the text-books. Of the cretin it should be said that while thyroid treatment may transform him physically into at least a semblance of normality, no such transformation mentally need be expected—he remains a defective. Hydrocephalics vary very greatly in their mental capacities. These special types constitute but a small percentage of defectives.

The physical "stigmata" on which at one time so much emphasis was laid as signs of inherent mental or moral degeneracy may also be passed over with but brief mention. Their significance singly is negligible, for their single occurrence is not infrequent in normal persons, but when they occur in any number from three upwards, they assume significance, not so much for diagnosis of the individual as for that of his family as probably degenerate. Our main reliance for guidance must, then, be found elsewhere than in the physical, and it will be convenient to pursue our lines of search in the order of: history, observation, and tests. Further, as consultation on mentality is most frequent either at the early ages from infancy to 7 years, and at the period of early adolescence, these two periods require to some extent separate treatment.

The Early Years.

History.—By history is meant individual history. Family history, however valuable, when obtainable in reliable form, as indicative of the presence of lunacy, deficiency, epilepsy, paralysis, functional nervous conditions as hereditary factors, is of no more value for a diagnosis of the individual than a plurality of stigmata. To appreciate the significance of individual history, it is necessary to keep before our minds certain norms of development as a guide to interpretation. Some of the main stages of physiological growth may be briefly epitomised.

Stages of Physiological Growth.—Within the first three months after birth a child, besides showing normal activity of the reflexes essential to life, should begin to take notice of objects affecting his various senses—noises, bright lights, tastes, and in some vague degree the more immediate objects in his environment—with, at the end of the period, some capacity to follow a bright object or turn towards a sound. The following three months sees considerable development of the power of seizing and grasping objects, with, towards 6 months, some little perception of their relative distance. At 6 months he can sit up, but will still require support, and his mother or nurse is now a fairly well-recognised entity. At 9 months a normal child can sit up without support, and will be crawling or otherwise propelling himself along the floor, and may even stand and try to step. About this time also are the first beginnings of imitation, but it is not a marked trait until the end of the year. Muscular coördination is now more reliable, both as regards grasp of objects and control of his own body movements. At 12 months he should walk with help, he will play with a spoon and a saucer and with blocks, but cannot construct; eye accommodation is now under control.

At 18 months he can walk alone, and even try to climb a stair, try to put on his shoes, and attempt to feed himself with a spoon. Bowel control should now be fairly reliable, followed at 2 years by bladder control. By 2 years he will build up a tower with three or more blocks. He can put on his shoes at 3, carry a frangible object, and open a door. At 4 he is mastering certain of the elementary processes of dressing—buttoning clothes and fastening shoes.

Language and Articulation.

Coincident progress in speech must be noted. After the early babbling stage comes, among other imitations at 8 or 9 months, the imitation of sounds heard, at first with no idea of meaning. Before 12 months a child should begin to understand what is said to him and to obey commands. Of use of actual words by himself at 12 months we expect little but "mama" and "dada" and a few other common baby words. A few months later he is appreciating the meaning of more words, but up to 18 months his own spoken vocabulary is extremely limited. The next six months, however, sees great extension in this direction, coupled with greater understanding. By 2 years he may have acquired as many as 200 words, and is a persistent imitator, so that echolalia is a marked feature at this stage. From this time the interaction of language and intelligence upon one another becomes more definite, and in the third year he is becoming acquainted with first the similarities of different objects, later their differences, and developing concepts consequently of wider and wider

* Part II., the Significance of Accepted Tests, will appear next week.

significance. Short sentences in place of single words, negatives, plurals, pronouns, parts of verbs make their appearance, and by the end of the third year that most significant of all mental advances, the use of the pronoun "I" is, in a normal child, well established. At the same time—and this is of importance—articulation should be nearly perfect.

Abnormalities in Development.

With these norms before him the assessor of intelligence has a fairly satisfactory basis for a diagnosis, provided that he can obtain approximately reliable data for the individual child before him. Retardation of teething, sitting up, and walking may only indicate rickets, of which there will be other signs, but when all these are combined with lateness in "taking notice" in infancy—a point soon discovered by an experienced mother—with absence of the normal babble, retardation of early efforts at speech, with, for a prolonged period, great difficulty of articulation, and lateness of other normal activities described, with late control of bladder and bowel, then there is a strong a priori case for a diagnosis of deficiency.

In the case of any child up to 3 and a markedly subnormal child to 5 (or even later) practically no other method of diagnosis but this and the observational is available, but at those early ages diagnosis must always be guarded. Idiocy and imbecility may be readily recognised then; such a child would probably not be talking at 3, and not very much and not distinctly at 5—to take only one sign as an example. But feeble-mindedness at these early ages is not so readily diagnosed. At any age up to 6 or 7 to say that a child who started to walk at 18 months and is only just beginning to talk at 2 to 3 years is not feeble-minded, and will be all right later, would be dangerous. Indeed, we may go further and say that a quite definitely feeble-minded child may only show a retardation of a few months in each of the activities above mentioned. More usual, perhaps, is a slight retardation in some and a marked retardation in one or two—say, talking or acquisition of cleanly habits. These inequalities are common in the feeble-minded, and the practitioner would be well advised to adopt a "wait and see" policy, a policy which, after all, he has to adopt in reference to many other diseased conditions. It is seldom indeed that a certifying officer will commit himself to say of any doubtful case until the age of 7 that the child is not feeble-minded.

With children of older ages the questionaire may be extended to present conditions—the child's ability to dress and wash himself, to bring a number of errands correctly by memory only, his play activities and hobbies, his propensity to play with children of his own age or younger, to be led by others, to defend himself against others. And, above all, a comparison either from the parents' own information or by actual testing, between him and a younger member of the family (if any) may be illuminating. In obtaining all this information, the practitioner—if he is the regular family doctor—has an advantage over the official certifying officer in that he has probably had opportunities of observing the growth of the child, and cannot, therefore, be so readily imposed upon by a parent anxious to cover up the facts.

Observation.

Much may be learnt by careful observation, and in the case of very young or very low-grade children it is practically the only method of examination that is possible. A vacant expression, a slouching posture, a clumsy gait are readily noticed. So also are rocking movements, biting nails, sucking the thumb, and other habitual purposeless movements, but they are not very common above the imbecile grade. Alertness and quickness to "take notice" or the opposite are usually obvious, and the child's ability to walk and to articulate clearly; his own attempts at spontaneous speech are often of significance. An abnormal amount of fidgetiness and restlessness in such degree that the child is on the move all the time, handling everything he sees, but only for a moment, distracted by the slightest interruption, is characteristic of one type of defective—the unstable. At the other extreme is the stolid type whom it is difficult to rouse to any activity, physical or mental. It is, of course, in the mass that all such signs find their meaning. They are, however, never all present—articulation, for example, is sometimes almost perfect even in a young imbecile.

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Senior Assistant School Medical Officer, Manchester Education Committee.

The Services.

ROYAL NAVAL MEDICAL SERVICE.

Surg. Comdr. F. Cock is placed on the Retd. List with rank of Surg.-Capt.

Surg. Lt. J. K. G. Way to *Victory*, for R.N. Infirmary, Portsmouth.

ROYAL NAVAL VOLUNTEER RESERVE.

Surg. Sub-Lt. J. O. Clyde to be Surg. Lt.

Proby. Surg. Sub-Lt. C. Seeley to *Victory*, for R.N. Hospital, Haslar, for training.

ROYAL ARMY MEDICAL CORPS.

Lt.-Col. H. H. Leeson, R.A.M.C., Res. of Off., to be Maj., whilst re-empld. under Art. 507 (b), Royal Warrant for Pay and Promotion, 1926, and relinquishes the rank of Lt.-Col.

The undermentioned Capts. to be Majs.: W. Bird, D. Cran, A. R. Ross, O. D. Jarvis, A. C. Taylor, R. Johnson, P. R. O'R. Phillips, T. H. Twigg, A. H. Clarke, D. J. H. Jones (prov.), J. K. Holland (prov.).

Lt. F. Welsh resigns his commn.

G. R. M. Apsey to be temp. Lt.

ARMY RESERVE OF OFFICERS.

Lt.-Col. J. D. Kidd to be Lt.-Col.

TERRITORIAL ARMY.

Lt.-Col. A. P. Watson to be Bt.-Col.

Capts. E. R. Woodroofe and A. H. Richardson resign their commns.

H. V. Ingram to be Lt.

Lt. E. White to be Capt.

2nd Lt. A. T. B. Dickson (late 7th Bn. H.L.I., T.A.) to be Lt.

TERRITORIAL ARMY RESERVE OF OFFICERS.

Capt. N. R. Rawson, from Active List, to be Capt.

INDIAN MEDICAL SERVICE.

Capts. R. S. Aspinall and Gangadrum Venkataswami Ram Mohan to be Majs.

P. J. Walshe, A. M. Sheridan, and J. H. Boultbee to be Lts. (on prob.).

Col. A. Spitteler and Lt.-Col. G. Fowler retire.

As will be seen from our advertisement pages the Secretary of State for India proposes shortly to make a certain number of appointments to permanent commissions in His Majesty's Indian Medical Service.

ESSEX PUBLIC MEDICAL SERVICE.—The fifth annual report (for the year 1928) of this Service shows that it provides increasingly for medical attendance on the families of insured persons. The number of subscribers rose from 14,594 in 1927 to 16,040 (7454 adults and 8586 children) in 1928, and their payments from £9427 to £10,446. The number of new books issued to subscribers during the year was 1904, and at the end of the year there were 8048 books on which payments were being made. The maximum remuneration of individual doctors during the year was, £371 in a metropolitan district, £720 in an urban, £244 in a semi-rural, and £231 in a rural area. The balance-sheet affords more cheerful examination than in any previous year for the excess of liabilities over assets is now only £132, with a prospect of disappearance next year. The loan from the National Defence Trust (originally £400) has been reduced from £400 to £300, and the doctors' loan from £100 to £55. The Service, whose offices are at 108, City-road, London, E.C. 1, has all the signs of a going concern.

LORD DAWSON OF PENN.

LORD MOYNIHAN.

RT. HON. C. ADDISON
(Wiltshire: Swindon).

DR. ETHEL BENTHAM
(Islington, East).

SIR GEORGE BERRY
(Combined Scottish Universities).

DR. A. VERNON DAVIES
(Lancashire: Royton).

MAJ. WALTER E. ELLIOT
Glasgow: Kelvingrove).

DR. ROBERT FORGAN
(Renfrew, West).

COL. F. E. FREMANTLE
(Hertford: St. Albans).

MR. H. C. HASLAM
(Lincolnshire: Horncastle).

Photos:
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Russell, London.
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Lewis-Smith, Chicago.
Dr. Addison—
Stuart Black, Torquay.

Photos:
Dr. Bentham—
Reprograph Studio.
Dr. Davies and Capt. Elliot—
Bassano.
Dr. Forgan—
Weir, Glasgow.

MEDICAL MEMBERS OF PARLIAMENT.

MR. SOMERVILLE HASTINGS
(Reading).

DR. JOSEPH HUNTER
(Dumfriesshire).

DR. E. G. GRAHAM LITTLE
(London University).

DR. H. B. MORGAN
(Camberwell, North-West).

DR. J. H. MORRIS-JONES
(Denbigh: Denbigh).

DR. DRUMMOND SHIELS
Edinburgh, East).

DR. ALFRED SALTER
(Bermondsey, West).

PROF. THOS. SINCLAIR
(Queen's University, Belfast).

DR. G. E. SPERO
(Fulham, West).

DR. J. H. WILLIAMS
(Carmarthen: Llanelly).

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Dr. Spero—
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MEDICAL MEMBERS OF PARLIAMENT.

Special Articles.

THIRTY YEARS OF SANATORIUM LIFE.*

BY ESTHER CARLING, M.D. BRUX., L.S.A.,
CHIEF MEDICAL OFFICER, BERKS AND BUCKS JOINT SANATORIUM.

THE coincidence of the Reading Pathological Society's visit to the Berks and Bucks Joint Sanatorium with the completion of 30 years of its existence suggests a backward glance and an inquiry as to how far the system still merits the confidence of the profession which feeds it.

The First Phase.

Systems of treatment develop from small flexible experiments into the hard concrete of the established order of things; with the acquisition of property, the appointment of officials, and the fencing around by legal documents an organisation comes into being which is very resistant to change. We have seen in the question of poor-law reform that, even when a Royal Commission has recommended action, over 20 years can elapse before the established order can be shaken. We see also how very slowly the structure of administration concerning mental disease is becoming modified. It is therefore surely wise to consider periodically the actual and relative values of any part of a system that has been on trial for a reasonable time, particularly if it happens to be a costly and exacting part.

Few practitioners will now remember the wave of interest that caught both the profession and the reading public when, late in 1898, a chemist named Gibson published in the *Nineteenth Century* an account of a cure for consumption which he had undergone in the Black Forest. This was followed by the experiences of several English medical men, and a rapidly spreading cult began for treatment on so-called Nordrach lines. Certain extravagances of Teutonic origin were at first included, and the overfeeding and lack of nursing of the Black Forest progenitor were part of the earlier English institutions. In 1899 several private sanatoriums were started, mostly by doctors who had themselves undergone the cure. The common-sense of a great deal of the system gained rapid support, and in a few years demand was forthcoming that the working classes should share the benefits. Here and there a specially wide-awake borough council or board of guardians made application to private institutions to start an industrial branch; employers asked for treatment for their servants or workpeople, and the demand for beds became insistent. Thus a very small experiment, started here in 1899, grew steadily by ones and twos. Patients were housed in huts and shelters with a minimum of capital expenditure, and year by year more and more pressure was made to extend the accommodation. There were certain dramatic moments when interested callers left cheques for £500, or when a deputation from a county council urged on us "sell your boots but provide beds." The stage of struggle and building up is ever the most vital and interesting. I often wonder whether the results which seemed so much better then than they do now were really so, or whether it was the youth and freshness and enthusiasm of all concerned and the newness of the system that gave such impetus and caused such quick developments.

The Edinburgh Dispensary and the Sequel.

The next step came with the development of the dispensary system organised in Edinburgh by Sir Robert Philip. The voluntary model so provided was rapidly copied and paved the way for the system which became a part of the public medical service with the National Health Insurance Act of 1911. From thence onwards local authorities, acting singly or in groups, have been building up their systems of antituberculosis work. As always in British procedure, a wide range of difference has marked the development. Some authorities have themselves developed a complete equipment with orthopædic provision, advanced hospital beds, and industrial colony, open-air day and boarding schools, after-care organisations, X ray plants in dispensaries, and "all the luxuries." Others have done little but farm out a few patients to voluntary institutions and spend as little as pressure from the Ministry of Health would allow. The sanatorium, which in early days was the star of first and greatest magnitude, has gradually become but one point in a constellation and there are signs that its brightness is still on the decline. As it is, however, by far the most costly single item, its relative value is worth determining.

An institution, such as the Berks and Bucks Joint Sanatorium for example, with 180 beds, costs the public something over £20,000 a year to run—and this amount represents an almost exact mean in the average cost of similar undertakings. The public asks very few questions, so also with the medical profession; the sanatorium just exists in the established order. Annual reports find their resting-place in the waste-paper baskets of county councillors; so long as no scandal occurs a deathly dullness envelopes it. Such lack of interest is unhealthy, but that is ever the trouble with public and official institutions that do not have to fight their way into the limelight.

The Basic Idea.

The basic idea of the sanatorium was that it afforded an opportunity for the "cure of consumption," and though this optimism has been modified by time presumably it should still offer some very definite values in return for the cost of upkeep. What these values amount to are best known by the body of general practitioners in the area which it serves, but probably it rarely occurs to them to criticise or consider the question as a whole, though they may have their general impressions. They would perhaps allow that a stay at the sanatorium does "some good," is "useful for a change," "gives the relations a rest," "teaches habits of hygiene," &c. We who live and work at the sanatorium hope it fulfils these functions and perhaps a few others, but we are also increasingly imbued with certain aspects of wastefulness and misdirection in the working of the scheme. For instance, we see repeatedly patients who have left the place full of hope and fitness returning in a year or two as physical wrecks, and we ask ourselves "was it worth while?" We realise often also that the short interval of health and working life that the sanatorium gave to these people has been the means of adding other handicapped lives to their families. This factor indeed is a problem which I think we have shirked far too much. The Parisians have faced it by a system of "placing out" the children born of tuberculous parents, but infant life is even yet more precious in France than in this country.

On the economic side comes the question: Is it worth while to give *so much* for a few weeks or months and *so little* for the remaining months and years of a very protracted illness? At the sanatorium is given a thoroughly ample, even generous, diet for example, and the patient is impressed that as he has lived at the sanatorium so should he "carry on" at home. He perhaps does not return to work, so the income is diminished. Yet he feels if he drops the generous feeding to which he has become accustomed his chance of maintaining the benefit gained is endangered, so he feeds up, and the healthy children have less that the invalid may have more.

Some of the Prospects.

A gradual development of late years calls also for comment. The average length of stay at the sana

* A paper read at a meeting of the Reading Pathological Society held at the Berks and Bucks Joint Sanatorium.

torium has steadily increased; in 1914 it was 12 weeks, in 1928 it was 28 weeks for adults (43 weeks children). This fact points to a change in the scope of the sanatorium. It has largely taken the place of the poor-law infirmary in dealing with chronic cases. This has some advantages: the life is on brighter, more vigorous lines; occupations are organised, crafts are taught, there are committees and interests, there is more coming and going. But there are also disadvantages; the buildings are not planned for the feeble chronic case. The advanced chronic patient is unnecessarily uncomfortable in winter and is a real anxiety to the staff lest harm should ensue. Some provision has recently been made here for "acutes," and it has been very helpful, but an entirely separate section would be a better way. Only rarely does the early case seek institution care, but the advanced should be encouraged to take it for the sake of others, and the middle cases for personal ends. Yet the sanatorium buildings are still planned on the lines which only the vigorous can reasonably profit by. If the sanatorium is sweeping all types into its net, what is it doing for them and what advances are recorded?

The sanatorium can always offer a helpful and educational "change," it can frequently initiate or carry through a useful course of special treatment; it can sometimes serve a moral or psychological purpose by altering a patient's outlook from invalidism to a more normal view, and there are indeed definitely some cases of a turning point to health again. It therefore seems to hold its own at present despite the degree of disillusionment which has been expressed.

In 30 years no specific treatment has arrived, and we are reminded of Tennyson's words:

> "Our little systems have their day
> They have their day and cease to be."

Tuberculin has had its day—and in some quarters it has still not ceased to be; serums have come and gone; vaccines have been tried and faded; heavy metals have still their advocates; surgical procedures have been in and out of fashion. Of late years the sun has come forth like a bridegroom from his chamber and has run a race with his ultra-violet derivative. Of all these one treatment at least has really been of lasting value in its own rather limited field, and that is the successfully established artificial pneumothorax. Some 253 cases have been undertaken here since 1911, and though the results are not sensational, they have meant a good deal in various ways.

1. The treatment offers a definite line of attack which, failing anything else, has a moral value. The old Devonshire saying "do good if you can but do zummat" has much wisdom in the treatment of a long disease like tuberculosis.

2. A pneumothorax course involves a régime of rest for a longer time than patience might hold out without a definite treatment.

3. When fairly complete compression can be established it has a really remarkable value. We have, indeed, on our staff to-day ex-patients treated by this means whose living and working seemed absolutely impossible four or five years ago.

The developments of the future seem likely to lie as much in the field of surgery as of specifics, and for this reason I hope that a "surgical side" will either become the rule at all large institutions or an alliance with the surgical departments of general hospitals. There is much to be said for grouping orthopædic and pulmonary cases on one area in different blocks as well as for dealing with all grades and types and ages. Just as in mental work the trend is towards larger units, so it might well be in tuberculosis. A more vigorous life for the staff is possible, and the larger the numbers the more efficiently and economically can a variety of needs be catered for. Another point is that the wider the range dealt with the less should the bogy of "infection" prevail. This is still a real hardship and disadvantage, yet a tuberculosis colony, wind-swept, sun-washed, and efficiently managed is a remarkably healthy spot in which to live.

The Tuberculosis Colony.

The sanatorium idea should move with the times, but at present it shows a tendency to stasis which is undesirable. From the first the idea of the *colony* has cropped up in varying forms—the "Nordrach colony," the farm colony, the industrial colony, all have had good examples and have shown certain possibilities. Finance generally wrecks them after a time; they can *not* be self-supporting. But the colony may come again, by wider groupings, by bolder planning, and by the welding of official and voluntary effort.

There is one element of "the colony" idea which is capable of very useful development—viz., the inclusion of a wide variety of children. It is very surprising that so few county units contain this provision; experience here shows that there is everything to be gained. The life of the children is quite separate, but they give brightness and vigour—they can be seen at play and heard shouting, and they make the place more homely. The teaching staff they need can give valuable help to the adults, and the medical resources called for in the diagnosis of their more indefinite symptoms also help the provision for the whole place. The criticism is often made, "But are they really tuberculous?" This is a nice point and one that I personally find increasingly difficult to determine. At any rate they are the weaklings of homes where tuberculosis has taken toll of adult members and they are wisely sent as a preventive measure. They yield naturally a fine harvest in immediate results, and I believe the tuberculosis officers who watch their later development are satisfied that these results are lasting. Certainly they very rarely return in adult life as patients. Whether they should be subjected to the label of notification as cases of phthisis is to my mind an important point, but it is a lesser evil to notify them than to withhold treatment. In looking back over the years, one feels that the children have been infinitely worth while. So also has been one other factor—the employment of patients as members of the staff. This has been done from the beginning wherever possible, and we are proud of the fact that some 40 per cent. of our staff are ex-patients. The advantage has not been all on their side—their presence is an encouragement to the patients, they bridge the gap that separates the worker from the invalid, and, further, they bring to the work conviction and enthusiasm engendered by their own success. If the fully fledged tuberculosis colony is an economic gamble too risky for public bodies to embark upon, the employment of ex-patients can at any rate be encouraged. Any technical difficulties they present as to insurance problems are worth overcoming. The mingling of normal and pathological workers calls for thought and care, but can be accomplished without harm resulting. On the economic side, if an institution can show about 40 per cent. of ex-patients on its staff and still keep a middle place on the cost list of comparative institutions, there cannot be much wrong.

I have perhaps said little on the strictly medical side, and my apology for this would be that in the long struggle with a disease like tuberculosis the medical side is less than the human, as the darkness of disease is less than the dawn of health.

KING EDWARD VII. HOSPITAL, WINDSOR.—Rapid progress with the rebuilding and extension of this hospital was reported at the annual meeting recently. The south wing will contain three wards in place of the former two; one of them is already occupied, and the other two will be available during the present month. Sir Edward Stern is adding an additional wing to the north ward, and the Lady (Gomer) Berry Hostel, which will be completed shortly, will contain nearly 100 rooms, about 80 of which will be occupied by the nurses. When this hospital is completed there will be 180 beds.

SCOTLAND.

(FROM OUR OWN CORRESPONDENT.)

Corporal Punishment.

THE question of corporal punishment having been raised before the Edinburgh Education Authority, a motion was made that, whenever corporal punishment was resorted to, appropriate particulars should immediately thereafter be recorded in an official record kept for the purpose. A committee on day schools and attendance considered this motion and disapproved of a recommendation by a subcommittee that the clause be inserted in the regulations. After discussion at a meeting of the authority the motion was defeated. Another motion was made that the regulation, "the Education Authority are very desirous that the infliction of corporal punishment should be avoided during the time set apart for religious instruction" should have added to it "and at all times in infant departments." This was also defeated. The intention of the first motion was to bring about a gradual abolition of corporal punishment, and there is in the procedure of the Central Board of Lunacy in Scotland, now the Board of Control, strong precedent for the method suggested. For here a special register having been instituted which required an exact statement of the particular reason, the nature of any restraint enforced, the length of time of the restraint and other particulars had the effect that the strait-waistcoat ceased to be used in the asylums of Scotland. No steps were ever taken, so far as I know, to abolish any form of restraint required; the recording of the details ended in the disappearance of this particular method. And it is probable that a register of corporal punishment in schools would have a parallel history.

The Scottish schoolmasters of former days were certainly not famous for their leniency in the use of the tawse, but possibly the belief in the disciplinary efficacy of an inflicted pain is a survival of the "possession" theory of wickedness, and those that accept that theory are becoming extinct. At the Edinburgh discussion, it was admitted by one supporter that the teachers of exceptional "personality" did not need to inflict corporal punishment, which is a comment of the first value.

The Glasgow Small-pox Outbreak.

In the bulletin of the Glasgow Public Health Department it is pointed out that only one case of small-pox was recorded last month. "This case was associated with the former outbreak in respect that the patient was a painter on the ship on which the infection occurred. He worked on board that vessel from April 20th to 23rd and was diagnosed on May 11th. He had been at work on another vessel from the date of his sickening on May 5th. All possible contacts were kept under observation and no further cases of the disease have arisen. It would now appear that the outbreak is definitely at an end." It is a matter of interest that no deaths have occurred among the cases which have arisen in Glasgow, but four small-pox patients remain under treatment. The case of the ship's painter forms an illustration of the variation in infectivity. The late Dr. John C. MacVail, whose knowledge of small-pox was extraordinarily extensive, used to tell with great humour the story of the Kilmarnock registrar who divided the population into two classes—those that had had small-pox and those still to take it! The story marks the difference between the administrative resources of those days and of these. Glasgow Public Health Department is to be congratulated on the rapid arrest of a rather serious outbreak.

Dundee Royal Infirmary.

At the annual meeting the chairman stated that, while over £80,000 had been added to the Endowment Fund, the income alone being used for administration, there had been a surplus in the reserve fund only in one year. This is the fund available for the general purposes of the institution. From that fund, which stood at £109,765 in 1918 and towards which £103,305 had been received during the intervening years, it had been necessary to draw a total sum of £161,663 to meet annual deficits, leaving the fund at Dec. 31st last at £51,407. This, he said, was face value, not actual value, and in view of the large additional commitments of the infirmary, it was clear that a large addition was required not to the annual income alone but to the total funds required for extraordinary expenditure. The infirmary is one of the finest general hospitals in Scotland and within the last few years many enlargements and improvements have taken place in it. In fact Dundee as a whole is peculiarly favoured in the number of public institutions supported by generous men of wealth, and the infirmary, from time to time, has shown great public spirit in taking on fresh burdens.

Presentation of Portrait to Sir Alfred and Lady Ewing.

On his retiring from the Principalship of Edinburgh University, a portrait of Sir Alfred Ewing was presented to the University and accepted by the Lord Rector, Sir John Gilmour, late Secretary of State for Scotland. A second portrait of Sir Alfred was presented to Lady Ewing. The Chancellor of the University, the Earl of Balfour, could not be present; but there was a large gathering representative of every phase of University work and interest in Edinburgh. The artist is Mr. Lintott, R.S.A.

Child Neglect.

The Scottish Society for the Prevention of Cruelty to Children does admirable work and it is no reproach to the "Children's Charter" that prosecutions successfully instituted by it may produce a situation which appears to render all effort nugatory. Here are four cases. A labourer, aged 33, pleaded guilty to having neglected his four children between Dec. 1st and May 29th and was sentenced to three months' imprisonment; a miner, aged 48, pleaded guilty to neglecting his three children and was sentenced to three months' imprisonment, admitting one previous conviction; a pit-head worker, aged 38, pleaded guilty to neglecting his six children between March 28th and June 3rd, admitting two previous convictions, and was sentenced to four months' imprisonment; another miner, age not stated, pleaded guilty to a charge of neglecting his wife and six children, and was sentenced to three months' imprisonment. Evidence of extreme laziness on the part of the fathers was forthcoming, and it is known that prosecutions are only instituted in the worst examples. In these cases the family, during the imprisonment of the father, has to be provided for by the poor-law authorities or by the Society, and the break-up of the family and the boarding out of the children may either or both be necessary. When the father comes out of prison, he resumes, whether he wishes or no, responsibility for his wife and children, and though kind efforts may be made to give him a fresh start he frequently returns with no work or wages to his family and the same results of laziness and incapacity follow. Many years ago, the Local Government Board for Scotland, then the central authority for poor-law, had to stop the inspectors of poor, acting under the Parish Council, from bringing the children to the prison door and handing them over to the father immediately on his release. This was then the conception of reinstating "parental responsibility." Possibly this variety of poor-law activity occurs from time to time still and no doubt, in the long course of handling worthless persons, the inspectors of poor have been driven to it as the sole method of "catching" the father and preventing his final desertion. But no one can regard this as a practical procedure. But in the four cases recorded above, it is difficult to know where to begin with a remedy, and with that difficulty the Scottish Society for the Prevention of Cruelty to Children is faced continually.

It is no wonder that the Society feels that the whole problem of the preservation of children should be be studied afresh, for police methods can deal only with the superficial aspects.

BERLIN.

(FROM OUR OWN CORRESPONDENT.)

The German Surgical Congress.

THE first official subject of discussion at the German Surgical Congress, which has lately been held in Berlin, was the treatment of empyema. Prof. Sauerbruch (Berlin) said that experience in the influenza epidemic of 1918 and 1919 had modified our views on the advisability of rib-resection for this condition, the mortality after resection having been 90 per cent. For post-traumatic empyema he thinks that a wide opening with removal of part of the ribs still gives the best results, but for para-pneumonic empyema and in empyema after influenza this method has nowadays fallen into disuse, and puncture of the pleura is performed instead. Its object is to improve the general condition of the patient, and this is often effected by a single puncture though several may be necessary. Should exudation continue, Bülau's drainage is recommended; and if, in spite of this, resection becomes necessary, the operation is less dangerous after the improvement of the patient's general condition. Prof. Sauerbruch holds that rib-resection must be done in a pressure chamber. Of 63 patients operated on under these conditions, 57 healed without a fistula and six died, whereas of 32 patients operated on without a pressure chamber 17 died. Where the lung is adherent to the parietal pleura an extrapleural resection of the ribs must first be performed; two or three weeks afterwards the pleura may be opened and the adhesion reduced.

The second official subject was the treatment of ureteric calculi. Prof. Voelcker (Halle) spoke of the difficulty of distinguishing the symptoms of calculus, cholecystitis, appendicitis, and ileus, to which end radiography is not always reliable. By catheterisation of the ureter the calculus may sometimes be brought back to the pelvis of the kidney. To reduce the pain caused by a calculus spinal anæsthesia may be tried; if there is no improvement ureterotomy with primary suture is necessary. Should the colic and retention of urine improve without removal of the calculi a condition resembling chronic cholecystitis is set up and there is a danger of the kidney being damaged by infection. Treatment then consists of the administration of suitable mineral waters by the mouth, with injection of oil or glycerine into the ureter. Prof. Voelcker did not approve of dilatation of the ureter according to Burger's method or of permanent catheterisation, which increases the chance of infection. Some calculi, he pointed out, are primarily infected—especially phosphatic calculi with a rough surface. In such cases intravesical therapy is undesirable; ureterotomy is indicated and the kidney may have to be removed. In acute anuria where catherisation of the ureter has not succeeded the kidney must be made accessible. If its condition is still pretty fair a renal fistula may be made through which the calculus will usually be discharged. If stones are present in both kidneys, and neither radiography nor ureteral catheterisation shows which is most affected, both must be made accessible so that the worse can be removed.

The third official subject, the treatment of adhesions in the abdominal cavity, was opened by Prof. Clairmont (Zurich) who showed a large collection of anatomical specimens illustrating different kinds of adhesions.

A Serological Blood Test.

Prof. Zangemeister (Königsberg) not long ago reported to the Berlin Medical Society on his experiments on blood-serum. It is known that by mixing the serum of two persons, the albumin being precipitated, the mixture becomes opaque. The degree of opacity, however, is sometimes so slight that it cannot be ascertained in the ordinary way. Zangemeister has therefore used the Tyndall effect, with Zeiss's photometer, which allows a very accurate measurement of the intensity of light. A mixture of the sera of two unrelated persons and a mixture of the sera of a mother and her child are at first equally transparent. But whilst the transparency of a mixture of the serum of the two unrelated persons persists, that of mother and child by and by decreases. A second test is made by the ultramicroscope, with which the illuminated albuminous substances look like stars in the heavens. In the mixed serum of mother and child the stars gradually conglomerate into large spots. The test proved reliable in the cases tested by Zangemeister, not only for mother and child but also for father and child, and not only for new-born infants but also for persons up to the age of 30.

Nationalisation of the Profession.

Between the municipal authorities and the medical profession in Berlin a conflict has arisen, which is of fundamental importance apart from its local interest. According to the Act concerning the campaign against venereal diseases the municipal authorities are obliged to take measures for the care of persons suffering from, or suspected of suffering from, such diseases. This provision has been complied with in many cities by the establishment of municipal dispensaries. Throughout Germany these dispensaries abstained from treatment, the patient being sent with a note to his club doctor or private practitioner after he has been examined. In Berlin alone have the dispensaries from the first undertaken treatment as well as diagnosis. By an agreement made in 1928 it was stipulated that the existing dispensaries might continue on condition that no new dispensaries were established by the city, but the Berlin municipal authorities have now given notice that they do not propose to be bound any longer by this agreement, which expires on July 1st, and that they feel obliged to open new dispensaries. Negotiations between the Hartmann-Bund and the city having failed, the Hartmann-Bund has declared a boycott of these dispensaries so that no medical man belonging to the Bund may apply for or accept an appointment in them. The boycott has been extended to other dispensaries too—for instance, those for tuberculous patients, and for mothers. The Hartmann-Bund states that already no more than 10 per cent. of the patients calling at municipal dispensaries are sent to private practitioners, the remainder being cared for in the dispensaries. Obviously the Berlin municipal council, which is under the influence of the Socialist Party, aims at complete socialisation of the medical profession, as has been observed on other occasions. The Berlin profession will fight against this tendency, for it is calculated to destroy the small residue of private practice which still remains.

According to a report by the Berlin Municipal Health Office, 67 per cent. of the children examined by the municipal dentists needed dental treatment. Children with healthy teeth are rare in Berlin schools, the cause being inadequate feeding.

The Cleveland disaster has caused some anxiety as to the possibility of a similar happening in one of the German hospitals. The Government has stated in the press that long before the Cleveland disaster instructions were given to the hospitals about the storage of films and their separation from combustible material. According to this statement it is highly improbable such a thing could happen in this country.

STOKE NEWINGTON HOME HOSPITAL FOR WOMEN.—Recently Princess Helena Victoria, the Patron, unveiled a tablet to the memory of Miss Isabella Lister, who was long closely connected with this hospital, which, with the exception of the visiting doctor, is entirely staffed by women. The institution was founded in the present building in 1825 by an aunt of the late Lord Lister, whose grandfather resided at Stoke Newington; Miss Isabella Lister was another relation. The Princess named the ward containing the tablet the "Isabella Lister Ward."

MEDICINE AND THE LAW.

A Coroner on Vaccination.

AT the adjourned inquiry on June 13th into the death of a woman of 31 following vaccination (the case is reported on p. 1302 of this issue) the coroner, Mr. Ingleby Oddie, in summing up remarked that this death, as well as another into which he had just inquired, was due to post-vaccinal encephalitis after primary vaccination performed later than in infancy. People, he said, apparently acquired the unknown germ of encephalitis after infancy; in many cases it was lying dormant and was excited into activity by some such stimulus as vaccination. Since in infancy there was presumably no germ of encephalitis yet present in the child's body, it would be better for all children to be vaccinated in early infancy instead of waiting until a small-pox scare caused them to be vaccinated later in life. In that way they would evade this risk of post-vaccinal encephalitis. Further, inasmuch as secondary and tertiary vaccination did not apparently result in encephalitis, it was worth considering whether that was possibly due to the slight local and general reaction occurring in those cases. If so, might it not be wise, he suggested, to try vaccination in all cases with fewer insertions and therefore less reaction? Possibly a less active—i.e., more dilute lymph—might not give rise to post-vaccinal encephalitis in primary vaccinations. Mr. Oddie expressed regret that coroners were not supplied with important documents such as the Rolleston report, of which, it seems, he had never heard. This particular report contained recommendations which might save many lives. Such highly important records of current research work should, he said, be furnished to the officials who are always dealing with deaths. On account of their expensive nature coroners did not see, for example, the annual reports of the Medical Research Council.

Operation at Wembley Hospital: Successful Claim for Fees.

There may be a popular impression that treatment in any kind of hospital means free treatment. Another county court decision in connexion with the Wembley Hospital, has, however, illustrated the practitioner's right to charge a fee for professional services in a case where the ordinary elements of a contract can be inferred. It is a common legal principle that the acceptance of a performance which has been requested will generally support the inference of a promise to pay a reasonable reward. As the Watford county court judge pertinently asked in the case to be discussed below, "Why should a doctor be presumed to do everything gratuitously?" In such a case as the following the important evidence is that which proves or disproves the employment of the practitioner by the person against whom the claim for fees is made.

Dr. J. A. Mackinnon, of Park-drive, Wembley, claimed 30 guineas from Mr. Henry King, of Berkhampstead-avenue, Wembley, for professional services. Plaintiff, who is on the honorary staff of the Wembley Hospital, attended defendant's wife in July, 1928, having been called into consultation by Dr. Cowardin. He decided that an operation was necessary, but, as the patient suffered from a definite heart disease, the operation was postponed and medical treatment was relied upon. In August, in Dr. Cowardin's absence on holiday, Dr. Mackinnon again attended Mrs. King; in September he saw her again and came to the conclusion that immediate operation was necessary to save her life. Her husband was not then at home. Dr. Mackinnon explained to her son that he would not take the responsibility of postponement for a single day. The son was asked to get into touch with his father; he did so by telephone, returning with a message that it was all right and that the operation should proceed. It was decided to remove Mrs. King to a private ward at the Wembley Hospital and no objection was taken to that plan. Dr. Mackinnon stated that he saw the defendant at the hospital that evening and made it clear that operation was the only means of saving Mrs. King's life; Mr. King replied "I am glad you have decided to do it." The operation was entirely successful and the patient was placed in the public ward, the private ward being full. Dr. Mackinnon had further conversation with Mr. King that night. Next day he attended Mrs. King, who had collapsed in the ward, and he obtained another nurse for her. The following day there was a vacancy in the private ward (in which, it is understood, there are four adult beds) but the patient preferred to remain where she was. In answer to the judge, Dr. Mackinnon estimated that he had attended Mrs. King at least twice a day for the 12 days she was in the hospital. In cross-examination he agreed that doctors in attendance who were members of the honorary medical staff should not charge a fee; but he did not agree with that rule as regards patients who could afford to pay. He was not asked by the hospital authorities to perform the operation. Dr. Cowardin gave confirmatory evidence for the plaintiff, and another witness remembered hearing Mr. King (in discussing expense) say that he was prepared to pay in moderation. The defendant said he earned £400 a year. He received his son's telephone message and had no alternative but to agree; he was not aware that the doctors were at that moment in his house. He had agreed with the hospital authorities to pay three guineas a week for his wife; he was told he would not have to pay anything for the operation. After hearing other witnesses for the defence, including the secretary of the hospital, the judge gave judgment for Dr. Mackinnon with costs, adding that he had not heard an action with a defence of less merit. He found that there was, in fact, a contract of employment for the performance of this particular operation and that the charge was fair and reasonable. It was a very serious operation which was completely successful; moreover the plaintiff's services continued afterwards. There was nothing to suggest that the defendant should not pay the plaintiff's fee. A number of side-issues had been introduced by the defence; whatever bearing they might have on the hospital authorities of the organisation of the medical profession, they had—said the judge—no bearing on the action before the court.

One of these side-issues was a desperate attempt to discredit Dr. Mackinnon by an accusation of dichotomy. He had stated in cross-examination that Dr. Jenkins was the anæsthetist and that Dr. Cowardin also assisted at the operation; they would receive three guineas each. The objectionable element in fee-splitting is, of course, the danger that fees are unnecessarily inflated by transactions between practitioners of which the patient is kept in ignorance. In Mr. King's case the judge (after hearing evidence at what he evidently regarded as excessive length) was satisfied with the fairness of the plaintiff's charges. To know which patients can afford to pay a fee, and to know what fee they can afford, may be a difficulty, but it is a difficulty which hospitals will have to face increasingly in future. Hospitals presumably do not desire to antagonise the medical profession, nor would they feel justified in asking the public to subscribe for the treatment of those who do not need charity. In the case under discussion two witnesses who sought to establish the defendant's case were the secretary of the hospital and the chairman of its house and finance committee; the solicitors for the defendant, it is believed, are also the solicitors for the hospital. If so, there is nothing improper or sinister in the alliance—least of all if it means that the hospital will make itself responsible for Dr. Mackinnon's costs. But the recurrence of these incidents at Wembley raises a suspicion of unfriendliness towards the medical profession which tact is needed to avoid.

Workmen's Compensation: Suicide following Nystagmus.

A miner contracted nystagmus in 1926. Three years later, after visiting a doctor (accompanied by the

branch secretary of the Miner's Federation) and after being told that he was still suffering from nystagmus, he disappeared and his body was recovered from a canal two miles away from his home. A claim was put forward by the widow in the St. Helen's County Court on June 12th. Evidence was given that, before he lost his health, the deceased was cheerful in temperament, but that, after contracting the disease, he grew morose and depressed. Some doubt was raised on behalf of the employers as to whether the deceased was actually suffering from nystagmus when he committed suicide. The Medical Referee held that the disease had turned his brain and caused him to take his own life. Suicide being thus regarded as a consequence of the nystagmus, the widow was awarded £400 compensation.

Merchandise Marks Act Prosecution: Coffee and Caffeine.

The magistrate at Bow-street on June 12th dismissed a summons against Wallace Pure Foods, Ltd., for having applied to certain tins of coffee, with intent to defraud, a false trade description. The tins were labelled "P. R." coffee, the initials standing for "Physical Regeneration." Labels stated that the coffee was "practically caffeine free, 100 ounces (representing 100 pints of liquid coffee) containing one-hundredth part of an ounce of caffeine." The prosecution's analysis indicated that caffeine from 3·37 to 3·7 grains per ounce was present, which was only a fraction less than the average amount contained in ordinary commercial coffee. For the defendants an analyst said that free caffeine might have been found in the coffee by analysis; but the analyst would have to obtain it from caffeine chlorogenate, a substance containing properties entirely different from those of ordinary caffeine salts. The magistrate accepted the defendant's contention that "caffeine" must mean "free caffeine" and not caffeine in conjunction with other substances. Experts for the prosecution had shown that, in order to obtain free caffeine, they had to break down the compound. This, said the magistrate, was a pale roasted caffeine (according to the label), and there was always more caffeine in dark roasted caffeine. On the dismissal of the summons an application for costs was refused. The prosecution mentioned the possibility of taking the matter to the High Court.

Tincture of Iodine.

An article which appeared in THE LANCET of Sept. 1st, 1928 (p. 443), was the subject of discussion before the Ealing magistrates on Thursday of last week, when Messrs. F. W. Woolworth and Co., Ltd., were fined £2 under the Food and Drugs (Adulteration) Act, and ordered to pay 10 guineas as costs for selling to an inspector of the Middlesex County Council "tincture of iodine" not compounded in accordance with the British Pharmacopœia, but consisting of a weak solution of iodine in isopropyl alcohol. For the defence it was stated that Messrs. Woolworths formerly sold tr. iodi mit., B.P., but last August were warned by the Excise authorities that the sale must be discontinued unless they had a spirit licence. The article by Dr. R. A. Macdonald and Mr. J. W. Peck, of the Great Ormond-street Children's Hospital, which appeared in THE LANCET soon afterwards, recommended a solution of iodine, 1·25 per cent., in isopropyl alcohol as an economical and satisfactory substitute for hospital use for skin antisepsis. This could be sold without a licence, and Messrs. Woolworths had been selling it labelled "iodine solution" since February. Among the witnesses for the defence was Dr. P. W. Boobbyer, of Ealing, who said that the solution was an excellently effective preparation which he would use himself without hesitation. Anyone other than a doctor who used iodine generally used 500 times as much as was required. The magistrates intimated that they thought that in selling the substitute when tincture of iodine was asked for, Messrs. Woolworths had been negligent, but not deliberately fraudulent.

Public Health Services.

REDUCTION OF TUBERCULOSIS IN LANCASHIRE.

THE Tuberculosis Committee of the Lancashire County Council has just presented a report showing the decrease in the number of deaths recorded from both pulmonary and non-pulmonary tuberculosis during 1928, as compared with previous years. The death-rate from *pulmonary* tuberculosis—namely, 0·58 per 1000 of the population—is the lowest on record in the administrative county for the sixth year in succession. For *non-pulmonary* tuberculosis the death-rate—namely, 0·15 per 1000—is also the lowest recorded for the county. Under the Public Health (Tuberculosis) Regulations, 1912, the total number of notifications of new cases of tuberculosis for the year 1928 in the administrative county is the lowest on record, as will be seen from the following table:—

Tuberculosis Notifications.

Year.	Pulm. tubere.	Non-pulm. tubere.	Total	Notifications.*	Year.	Pulm. tubere.	Non-pulm. tubere.	Total	Notifications.*
1913..	2700	1592	4292	1·54	1921..	2044	899	2943	1·16
1914..	2820	1140	3960	1·61	1922..	1863	956	2819	1·05
1915..	2872	1128	4000	1·64	1923..	1937	1188	3125	1·09
1916..	2689	1180	3869	1·52	1924..	1972	1120	3092	1·10
1917..	2375	1062	3437	1·35	1925..	1846	1027	2873	1·03
1918..	2534	885	3419	1·47	1926..	1828	953	2781	1·02
1919..	2105	847	2952	1·21	1927..	1794	1045	2839	0·99
1920..	2084	968	3052	1·20	*1928..	*1660*	*956*	*2616*	*0·91*

* Number of notifications of pulmonary tuberculosis per 1000 of population.

The improvement, it is pointed out, is really greater than the figures show, as in the earlier years there is no doubt that a considerable number of cases escaped notification. This is proved by the fact that in 1918 there were 303 deaths from pulmonary tuberculosis in which the case had not been notified, whereas during 1928, with general greater efficiency in rendering notifications under the regulations, the figure dropped to 56.

The decline in the number of deaths recorded, and of new cases of tuberculosis notified in 1928, has taken place despite the serious amount of unemployment in the staple industries.

INFECTIOUS DISEASE IN ENGLAND AND WALES DURING THE WEEK ENDED JUNE 8TH, 1929.

Notifications.—The following cases of infectious disease were notified during the week:—Small-pox, 272 (last week 242); scarlet fever, 1614; diphtheria, 929; enteric fever, 41; pneumonia, 1014; puerperal fever, 36; puerperal pyrexia, 110; cerebro-spinal fever, 14; acute poliomyelitis, 2; encephalitis lethargica, 22; dysentery, 6; ophthalmia neonatorum, 112. No case of cholera, plague, or typhus fever was notified during the week.

The largest incidence of small-pox at the moment is in London (Bethnal Green, 15; Shoreditch, 11; Stepney, 30); Blackwell R.D. (Derby), 15; South Shields, 11; West Ham, 28; Northampton, 16; Stoke-on-Trent, 24; Spenbury (Yorks), 6; Pontefract R.D., 8.

The number of cases in the Infectious Hospitals of the Metropolitan Asylums Board on June 11th–12th was as follows:—Small-pox, 301 under treatment, 14 under observation (last week 286 and 16 respectively); scarlet fever, 1348; diphtheria, 1525; enteric fever, 16; measles, 154; whooping-cough, 583; puerperal fever, 30 (plus 10 babies); encephalitis lethargica, 119; "other diseases," 51. At St. Margaret's Hospital there were 18 babies (plus 10 mothers) with ophthalmia neonatorum.

Deaths.—In the aggregate of great towns, including London, there was no death from small-pox, 4 (1)

from enteric fever, 63 (3) from measles, 4 (1) from scarlet fever, 32 (6) from whooping-cough, 21 (6) from diphtheria, 48 (5) from diarrhœa and enteritis under two years, and 53 (6) from influenza. The figures in parentheses are those for London itself.

Liverpool reported 20 deaths from measles, Leeds 9, and Birmingham 5. Leeds stood highest with 3 deaths from whooping-cough. Diarrhœa accounted for 5 deaths in Liverpool, 4 in Nottingham, and 3 each in Birmingham, Leeds, and Sunderland. Birmingham reported 4 deaths from influenza.

The number of stillbirths reported during the week was 264 (corresponding to a rate of 35 per 1000 births), including 53 in London.

REPORTS OF MEDICAL OFFICERS OF HEALTH.

THE following are 1928 statistics of two sea-port cities and a county:—

Name of district and estimated (R.-G.) population.	Birth-rate.	Death-rates per 1000 of the population.					Death-rates per 1000 births.		
		All causes.	Tuberculosis.	Cancer.	Respiratory diseases with influenza.	Heart disease.	Infant and neonatal mortality.	Young child (1–5 yr.) mortality.	Maternal mortality from childbirth.
Plymouth .. (211,980)	17·0	12·0	0·90	1·52	2·1	1·3	69/34	38	6·0
Aberdeen (City).. (159,954)	20·7	14·0	1·05	1·55	1·8	—	94/38	43	7·5
Aberdeen (County).. (105,713)	21·9*	13·4	0·97†	1·29	1·6	—	63/—*	—	4·2‡

* Amongst a population of 120,801, including 8 of the 10 burghs.
† Amongst a population of 143,191, including the 10 burghs.
‡ From puerperal sepsis only.

Plymouth.

Dr. A. T. Nankivell mentioned last year that extension of maternity and child welfare work would be not only desirable but also popular with the citizens. This increase has not yet been accomplished, but Dr. Nankivell hopes that before long it will be forthcoming. Some of the practitioners in Plymouth view with apprehension this extension and that of the school medical service, and Dr. Nankivell goes on to point out how very much better from a financial point of view it is for the panel doctors to have charge of patients whose health has been well supervised in their youth. An increase in the medical staff is needed not only for extensions but for meeting sickness absence, holidays, and emergencies. There were 28 cases of mild small-pox with no deaths, and Dr. Nankivell welcomes the provision of the new hospital at Lee Mill which is now nearing completion. Among other matters which indicate the progress in 1928 are: The completion of the central laundries for the corporation hospitals; the opening of a new block for boys at Didworthy sanatorium; the installation of an X ray plant at Beaumont House tuberculosis dispensary; the provision of a new motor-ambulance, and the sanction of the Ministry for the treatment of 40 cases of intermediate and advanced tuberculosis in women at Swilly Hospital.

Health education has received much attention. 132,000 copies of the magazine "Better Health" were distributed. As an example of the usefulness of the latter, a case is quoted where a woman consulted her doctor early as the result of listening to an article read by her son on cancer. The articles in "Better Health" are used for essays and lectures in the schools. The municipality own a number of cinematograph films, which were exhibited thousands of times at the theatres and cinemas. The "Runsyne" machine with its illuminated messages on health subjects has been operating in two positions during the year. Much educational work was carried out at the Health Exhibition in the Drill Hall during a week in July. Dr. Nankivell mentions that there have never been so few deaths from tuberculosis as in 1928, but that there is a marked increase in cancer mortality. He thinks the slow disappearance of tuberculosis is chiefly due to the facts that the disease is naturally dying out, that the standard of living is getting better, that the people are becoming more educated, and that the activity of tuberculosis schemes is increasing. Plymouth has much house property of so poor and decadent a nature that it is not reasonably fit for human habitation. The reconditioning work done during 1928 is described but, says Dr. Nankivell, only the fringe of the housing problem is touched as yet, and the fact that we are now suffering from the want of foresight of our great grandfathers is no excuse for inertia to-day. Dr. Nankivell looks forward to a great improvement in the hospital facilities of Plymouth when the poor-law is taken over next year.

The yield of oysters from the Tamar beds shows a reduction in recent years, and there is reason to believe that the beds have been overdredged and should be given a rest for several years. The oysters obtained, owing to the pollution of the Tamar, are replanted in the Yealm and Helford rivers until ready for sale. The purity of the Yealm is being threatened by crude sewage from the new houses springing up on its banks. The attempt to breed oysters in the Yealm has up to now been a failure.

The municipal slaughter-house ("an unseemly and inadequate place") is to be closed, and a new modern abattoir with proper cold storage in the neighbourhood of Prince Rock is strongly urged. This question has been discussed without result for a quarter of a century.

Aberdeen.

The acting medical officer of health, Dr. George S. Banks, states that the present report is mainly a statistical survey, the results of various experimental investigations of the health department having been incorporated in the 1927 report. The figures for 1928 bring out the greater relative fatality of measles and whooping-cough. Thus there were 728 notifications of scarlet fever with 5 deaths, a case-fatality of 0·7 per cent.; there were 458 notifications of diphtheria with 15 deaths, a case fatality of 3·3 per cent.; the cases of measles known to the health department numbered 1812 with 50 deaths, a case-mortality of 2·8 per cent.; while the cases of whooping-cough reported numbered 579 with 37 deaths, a case-mortality of 6·4 per cent. Out of 15 notified cases of paratyphoid B, 6 occurred in an institution as the result of infection by a carrier. The immunisation scheme makes progress and during the year 1704 children were immunised at the welfare centres and 2646 in the schools simultaneously against diphtheria and scarlet fever, while 665 out-patients were similarly dealt with. The case-notes are given of an unusual attack of continued fever caused by *B. alkalescens* (Andrewes). The illness ended in recovery after about six weeks in hospital. It is estimated that of the 168 deaths from tubercle, 92 per cent. were due to the human bacillus and 8 per cent. to the bovine. Of 90 samples of milk examined, 6, or 6·7 per cent., contained tubercle bacilli, while the average percentage for the years 1923–27 was 5·7.

In January an outbreak of septicæmia occurred in a maternity institution which had provision for 26 maternity beds and 8 antenatal cases. The wards were considered to be overcrowded and relief was given by the admission of patients to the municipal hospitals. Twelve mothers developed puerperal fever within a period of 5 weeks and 4 died. The outbreak was due to hæmolytic streptococcal infection. Concomitantly there was an outbreak of

icterus neonatorum with 7 infant deaths, and the *S. hæmolyticus* was found post mortem. Examination of the "contact" mothers revealed the *S. hæmolyticus* in the uterus and throat of one, in the uterus of 4 others, and in the throat of 3 others. Out of 12 nurses, 5 gave positive results from throat cultures. Some of the findings of the report of the Scottish Board of Health on maternal mortality in Aberdeen 1918–27, published in 1928, are given. It is suggested, amongst other things, that the high incidence of puerperal sepsis in maternity institutions in Aberdeen is due to contagion, and that the higher incidence of puerperal sepsis in the practice of doctors as contrasted with that of midwives is due, partly, to a streptococcal carrier condition in doctors. Of 3423 live births, 652 were attended by midwives; 603 as in-patients and 194 as extern patients by the maternity hospital; 1972 by medical practitioners, and 2 were unattended. There were 25 deaths of women associated with pregnancy and childbirth, including all deaths within four weeks after childbirth or later if the illness originated in the puerperium. In 4 the confinement was attended by a midwife; in 9 by the maternity hospital; in 7 by medical practitioners; and in the remaining 5 by other institutions. In 12 of the cases the fatal confinement was the first.

The undertaking with the parish authorities to admit all the sick poor to Woodend Hospital was occasionally difficult to fulfil, but no pneumonias were refused admission to hospital. There were 110 lobar pneumonias treated in hospitals with 7 deaths, 76 broncho-pneumonias with 12 deaths, and 7 influenzal with no deaths. One butcher, who sold a carcass of a pig grossly affected with tuberculosis to another, was fined £20 and the recipient of the pig £5. The sunshine record was 1227 hours, as compared with an average of 1285 for the previous 30 years.

A table giving a comparison of the statistics of the six principal Scottish towns shows that the standardised death-rates from all causes were: Edinburgh, 13·9; Aberdeen, 14·1; Paisley, 14·4; Dundee, 15·1; Glasgow, 16·7; and Greenock, 17·1; and that the infant mortality-rates were Edinburgh, 75; Aberdeen, 94; Dundee, 102; Paisley, 105; Glasgow, 107; and Greenock, 120.

Aberdeen County.

Dr. Harry Rae (who has since been appointed M.O.H. for the city of Aberdeen) reports that the immunisation scheme against diphtheria and scarlet fever is being continued, but that this work in a rural area must be more or less sporadic unless a special medical staff is employed. In addition to the schools immunisation has been used for the employees of three dairy farms which supplied Certified Milk. Retesting is found to be very necessary, but during the year there were only three notifications of diphtheria among children who had been inoculated. In order to obtain a higher immunity against scarlet fever four injections are being used instead of three, the fourth being one of 5000 skin test doses. It has been found that immunity against scarlet fever is usually established 14 days after the last injection. This scarlet fever immunisation may prevent the occurrence of "return" cases, whilst the same cannot be said of diphtheria, in the case of which immunity takes from six weeks to six months to develop. In order to prevent "return" cases of diphtheria, passive immunisation by 2000 units of antitoxin is recommended. The dosage laid down for the treatment of diphtheria is 4000 units for the first day of illness, 6000 units for the second day, and 8000 for the third day.

A county institution had one fatal case of typhoid fever in April and contemporaneously, an outbreak of ten cases of paratyphoid B, which appeared to be associated with a carrier in the kitchen staff. At the end of August there was a sudden outbreak of infantile paralysis chiefly in the neighbourhood of Fyvie. There were 13 cases in all, with one death. Three of the cases occurred in areas distant from Fyvie. Of the ten Fyvie cases three occurred in one family and two in another. Social circumstances and milk-supply had no bearing on the outbreak. The diagnosis was confirmed by the examination of the cerebro-spinal fluid. One of the two cases in one family had a previous attack six years ago, on which occasion paralysis of the leg appeared five weeks after the initial illness. After the second attack there was paresis of the left arm. The particulars of this case were confirmed by the records of the county public health department and of the city hospital. A previous outbreak of this disease occurred in the city from April to September, 1916, when there were 79 cases and 4 deaths, and coincidently 16 cases in the county with no deaths. In the 1916 outbreaks there appeared to be no connexion between the cases except in two households where there was a second case, and the households affected were chiefly of good social status.

The housing position shows progress in the provision of new houses. Dr. Rae is enthusiastic as to the advantages of the Housing (Rural Workers) Act, 1926, and thinks it is the only Act which will stem the tide of rural depopulation. Under this Act there were only 50 applications in 1927, whereas in 1928 there were 126, 43 of which were dealt with by the Deer District Committee. Dr. Rae goes on to point out that the Act is not limited to the housing of agricultural workers, but applies to those with similar financial resources, and is also applicable to burghs. He urges every burgh to adopt the Act, and further emphasises the powers given by many housing Acts to local authorities to purchase and reconstruct dilapidated properties, which can then be let at rentals within the reach of the poor. In many of the burghs owners of houses are financially unable to put them in habitable repair according to present-day standards.

The county veterinary inspector points out that with the present staff it is only possible to visit the dairy farms in the widespread area of the county once a year, and that a more frequent inspection is necessary for the detection of tuberculosis. In Aberdeenshire many of the cows are bought newly calved and only retained in the herd for one lactation. It follows, therefore, that many cows enter and leave a herd during the course of a year without ever having been seen by the veterinary inspector. During 1928 the inspector discovered 21 cows with tuberculous mastitis, which were dealt with under the Order. In three notified cases of (human) non-pulmonary tuberculosis the evidence appeared to incriminate certain milk-supplies, and the veterinary inspector found that two of the patients had been supplied with milk over a prolonged period from farms where there were cows suffering from tuberculous mastitis.

SOCIETY OF MEDICAL OFFICERS OF HEALTH.—The Neech prize offered annually for the best paper read before a branch or group of this Society has been awarded for the session 1927-28 to Dr. H. Stanley Banks, medical superintendent of the City Isolation Hospital, Leicester. Dr. Banks's paper was on the Intensive Serum Treatment of Severe Diphtheria, and was read before the Fever Hospital Medical Service Group of the Society. A paper on the same subject by Dr. Banks and Dr. George McCracken appeared in THE LANCET of July 7th, 1928 (p. 4).

The annual provincial meeting of this Society will be held at the Sedbury Park Hotel, near Chepstow, on Saturday, June 29th, at 10.30 A.M., when Dr. E. Colston Williams (county medical officer for Glamorgan) and Dr. R. M. F. Picken (medical officer of health for Cardiff) will open a discussion on the Medical Aspects of the Local Government Act, 1929. After lunch members will motor to Chepstow Castle, Tintern Abbey, and Raglan Castle, and thence to a garden party at Llanover Park, by invitation of Lord Treowen, Lord-Lieutenant of Monmouthshire, and Lady Treowen. The full programme may be found in the current issue of *Public Health*.

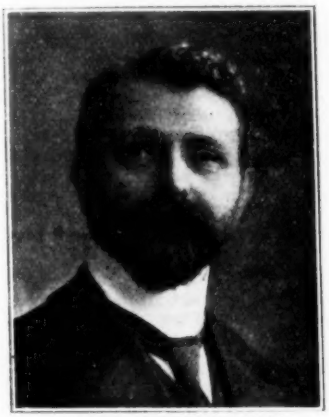
Corrigendum.—We regret an error which occurred in the obituary notice last week of Sir William Fairbank. Mr. H. A. T. Fairbank is the son of the late Dr. Thomas Fairbank, the elder brother of Sir William.

Obituary.

SIR WILLIAM THOMPSON, M.D. DUB.,
FORMERLY REGISTRAR-GENERAL FOR IRELAND.

THE sudden death of Sir William Thompson on the night of June 10th caused a sense of personal loss to the whole medical profession of Dublin, as well as to a large circle of friends. After a day of usual activity, and presenting no evidence of ill-health, he retired to bed, and was found dead next morning. He was 68 years of age.

Thompson was born in the north of Ireland, but spent his whole life from boyhood in Dublin. As a young man he entered the Civil Service, but shortly abandoned it for medicine, and qualified in 1888 with the double diploma of the Irish Royal Colleges. Six years later he proceeded to the degree of Bachelor of Medicine of Dublin University, took the M.D. degree in 1895, and became a Fellow of the Royal College of Physicians in 1902.



SIR WILLIAM THOMPSON.
Photo by Lafayette.

In his earlier professional life Thompson was engaged in general practice, but soon was elected physician to Jervis-street Hospital. He resigned medical practice in 1909 on his appointment as Registrar-General for Ireland, in which office he continued until his retirement under the age rule three years ago. During the second Vice-Royalty of Lord Aberdeen he was one of the physicians to the Lord Lieutenant, and during his tenure of this post he came prominently before the public eye. For Lady Aberdeen decided to organise a campaign for the improvement of health in Ireland, and, in particular, to fight against tuberculosis, and in this campaign Thompson was her chief adviser and right-hand worker. He showed an energy and power of organisation which had hitherto had little scope, and the success of the campaign in educating the public of Ireland, and in reducing the mortality from tuberculosis, is largely due to his energy and gifts. In work of this kind he remained indefatigable up to the day of his death.

In 1925, having filled various other offices, he was elected President of the Royal College of Physicians of Ireland, and the following year saw his retirement from public office, since when he devoted the whole of his time to voluntary philanthropic work. The Women's National Health Association, the Sanatorium for Tuberculosis at Peamount, Sir Patrick Dun's Hospital, the Royal Victoria Eye and Ear Hospital—these are only a few of the institutions where he expended his energy. He was a working member of innumerable committees, and everywhere that he worked his common sense, his business capacity, and his good humour made his help effective. He will long be missed on the executive of these and other philanthropic and humane undertakings in Dublin. For his gifts of adaptability, geniality, and good-heartedness made him the most pleasant of colleagues.

At his funeral, which was held at the Centenary Methodist Church, St. Stephen's Green, Dublin, on June 13th, all the numerous institutions and associations which he had served so well were prominently represented, among a large assembly of friends and the general public.

Correspondence.

"Audi alteram partem."

EXAMINATION OF TUBERCULOSIS CONTACTS.

To the Editor of THE LANCET.

SIR,—I have read with great pleasure your leading article of June 8th and the criticisms of it last week. If Sir Robert Philip and Dr. Fanning will pardon me I think they have taken the lighter parts of the article far too much to heart. At various periods I have had charge of a children's sanatorium and there is nothing I think sadder than the thought that probably 90 per cent. of the little patients had no tuberculosis at all and yet they had been notified and thus stigmatised for life. Every central tuberculosis dispensary ought to have a good X ray plant, but in many ways it would be dangerous as many more children would be sent to sanatoria simply on hilar shadows, if the tuberculosis officer has an idiosyncrasy in that direction. Obviously we do get pulmonary tuberculosis in school-children with tubercle bacilli in their sputum, but they are extremely rare. The omnibus expert and the pseudo-sanatorium are the two outstanding blots on all tuberculosis schemes. Abolish them and the "contact" and other questions will right themselves. There ought to be many more convalescent homes for debilitated contacts.

I am, Sir, yours faithfully,
JAMES D. MACFIE.

Winsley Sanatorium, near Bath, June 15th, 1929.

To the Editor of THE LANCET.

SIR,—It is perhaps natural that the first paragraph of your leading article of June 8th should have provoked indignant replies from those who practise and preach the doctrine of examination of contacts. Even those of us who are very sceptical about its value as a preventive measure would nevertheless hesitate to recommend that this practice should be dropped. The careful examination and following up of the families and contacts of tuberculous persons, while, in the experience of most tuberculosis officers, it fails to detect symptoms of tuberculosis which anyone with an ounce of scientific scepticism would regard as significant, is gathering for us over a long series of years just that information necessary to establish a sound knowledge of the natural history of the disease which at the present time tends to be theoretical and founded on analogy with the pathological course of the disease in animals. Here is a group of persons willing in their own interest to submit themselves to examination, some of whom are certain to present manifest signs of tuberculosis sooner or later. The opportunity of watching their progress should not lightly be thrown away.

It is a fact that the great majority of cases of pulmonary tuberculosis which come under the notice of a department for the first time are not associated by familial or other contact with any previous known case. Further, those cases which do come of tuberculous families are very frequently unrecognisable as cases of tuberculosis even of an incipient character during the period over which it is reasonably practicable to submit most of them to continuous examination and supervision. For the reason already given it is desirable to extend the period of observation indefinitely in as many cases as possible, but if the results are to be of practical value the selection of cases for such observation should not depend on the presence of some evidence that the individual so selected is already prone to develop the disease. The obstacles to such a line of study are, of course, obvious to all whose function is the detection and cure of disease.

Since ever measures specifically directed at the eradication of tuberculosis have been discussed, there has been difficulty in balancing the two arms of attack—viz., prevention of infection and stimulation of resistance to it. The pendulum has swung

one way and then the other. The inevitable result of the enthusiasm of the sanatorium specialists in the first decade of this century naturally led to the inauguration of schemes for early detection of cases and their submission to open-air treatment. An essential part of such schemes was the examination of contacts, and, of course, if the signs and symptoms are sufficiently indefinite it is possible to get very good results by this means. But, as a result of the work of the very sound and able clinicians of whom the tuberculosis service is now composed, there appears to be a swing back to the importance of preventing the spread of infection by isolating the advanced and highly infectious forms of the disease. The facts presented by Dr. Lissant Cox as to the incidence of tuberculous meningitis in the infants of infected households are an illustration of the influences coming to bear on the problem.

Obviously, we must lose nothing which we have gained by the intensive study of sanatorium treatment since 1912, but one of its most important lessons seems to be that the boosting of resistance should be applied before symptoms of any kind have appeared, and should not merely be confined to the suspected contacts of known cases of tuberculosis. Indeed it is a question affecting the general health of the community and depends as much on the education in hygiene of the healthy as of the suspected, since the latter must suffer for the communal sins of the former—as witness the problems of ventilation even in the office of a medical officer of health.

I am, Sir, yours faithfully,

RALPH M. F. PICKEN,
June 17th, 1929. M.O.H. and School M.O., Cardiff.

To the Editor of THE LANCET.

SIR,—Your thoughtful and timely comments on the report of Dr. Lissant Cox and the Lancashire Group of Tuberculosis Officers include criticisms of contact examinations as carried out at dispensaries with which many, though not all, tuberculosis officers will agree. But the criticisms hardly apply to home visits and contact examination in the home. If the tuberculosis officer makes a routine visit to the home of every patient, notes the conditions of life there, writes down the names of all members of the family as well as others exposed to infection, and reviews, or inquires about, the health of each, the procedure is by no means futile; for—

(1) He is enabled to suggest useful readjustments in the patient's mode of life and endeavour to prevent infection.

(2) He may discover delicate children and benefit them by preventorium treatment.

(3) An unsuspected source of infection is sometimes noted.

(4) Occasionally a case of active major tuberculosis is found and treatment initiated. It is true that a number of cases with a few physical signs and symptoms will be seen who do very well at home with no special treatment; but experience helps to indicate what line should be followed in such cases.

(5) He notices what is disclosed in this report—the frequency of non-pulmonary tuberculosis in the households of tuberculous patients.

Some of this work can be done by the health visitors, but their services are perhaps more useful in following up cases and assuring, as far as possible, that patients act, and continue to act, according to instructions. The best potential preventive agent is the general practitioner, but the tuberculosis officer can help him considerably, without friction and without causing the patient to lose confidence in his adviser.

I am, Sir, yours faithfully,

Paignton, June 14th, 1929. ERNEST WARD.

To the Editor of THE LANCET.

SIR,—I read with great interest the first paragraph of your leading article of June 8th, and congratulate you on your courage. We have, in the Administrative County of Lancaster during the last 14 or 15 years, found that the examination of contacts is a matter of the greatest importance. But the contacts require to be selected. Thus, in the Administrative County in the last three years we have examined 3947 contacts, of whom 253 (168 pulmonary and 85 non-pulmonary) cases were definitely diagnosed as tuberculous; 33 per cent. of the pulmonary cases had a positive sputum. Clearly, as your writer pointed out, a large proportion of such contacts are above school age. Your paragraph concludes with the sentence: "The so-called 'tuberculous seedling' is not the precursor of the consumptive adolescent who from diffidence or pressure of business is usually reluctant to attend the dispensary as a contact." Our experience entirely supports this view. Further, our administrative arrangements as to the proportion of beds for adults and children are based upon it. Thus, 91·6 per cent. of pulmonary beds are reserved for adults, and we save much money by having but few beds for children supposed to be suffering from tuberculosis. Out of part of this saving we are able to devote more money to provide the tuberculosis officer with up-to-date diagnostic facilities—e.g., X ray apparatus—and also to pay salaries which will attract highly skilled officers. In short, we lay the greatest stress on accurate diagnosis and isolation of adult infective cases.

I am, Sir, yours faithfully,

G. LISSANT COX,
June 17th, 1929. Central Tuberculosis Officer, Preston.

*** We print on p. 1326 an extract from Dr. Cox's report to the Lancashire County Council giving the results of the Tuberculosis Committee's scheme.—ED. L.

PAYING A PATIENT'S BILLS.

To the Editor of THE LANCET.

SIR,—As the defendant in the action, Maley *versus* Churcher, certain features of the case struck me forcibly. Never have I been so surprised at reluctance to pay an account. A young schoolmaster is found one evening lying on the floor of one of the school bathrooms with a large wad of cotton-wool soaked with ether over his face. The scholars are mostly foreigners, boys and girls, thoroughly scared at this development. At his own request, the patient is sent home by car in the charge of a nurse. Neither will the father, who has his son home safe and sound, nor will the principal, who has had the cause of the upset in her school removed, pay for the hire of the car. The only application for payment made to me was a curt solicitor's letter stating I was liable for the hire of the car, and that failing immediate payment proceedings would be started. This was the first definite information I received that the car had not been paid for.

This case illustrates once again the value of membership of one of the medical defence societies. The solicitors of the Medical Defence Union came down to Eastbourne, with counsel, to contest the case, and did their unavailing best. Two appeals have failed to reverse the decision. It would have been very simple to have paid the £5 when first demanded, but a principle appeared to be at stake. The case was well worth fighting, even if the result was defeat. I have to pay the car hire and the Medical Defence Union the costs of both sides throughout the case. As a profession we now know that no one need suppose that a doctor is acting as an agent for his patient, unless with one and every order an explicit statement of such agency is made.

It may be mentioned that the school was only a holiday one, not one of the Eastbourne resident schools, and that my account for professional attendance remains unpaid.

I am, Sir, yours faithfully,

D. G. CHURCHER, M.D., F.R.C.S.
Eastbourne, June 17th, 1929.

*** We protested vigorously last week against the continued operation of legal rules under which the decision against Dr. Churcher was possible.—ED. L.

WOMEN'S HOLIDAY FUND.

To the Editor of THE LANCET.

SIR,—At a time when discussion of holiday plans is heard in all directions, and the eye is met by posters urging one to travel abroad or to take one's holidays in June, may we be allowed to remind your readers of the many poor women in London who get little or no relief from the monotony and drudgery of their daily lives? Last year the Women's Holiday Fund sent away 1025 women and 377 children for a fortnight's holiday to the seaside. The committee hope to be able to assist at least as many this year, provided they receive the same generous support. £3 is the average cost of a fortnight's holiday, but a gift of £2 will ensure one woman having a holiday, as the applicants contribute about one-third of the cost. It is unnecessary to dwell on the value of a holiday to those coming from poor and in many cases sadly overcrowded homes, and particularly to the wives and mothers on whom the burden and strain of life rests most heavily. The experience is, as many of them express it, "like a bit of heaven," especially when it is the first holiday of their lives. Subscriptions, large or small, will be gratefully received and acknowledged, and should be sent to the Secretary, Women's Holiday Fund, 76, Denison House, 296, Vauxhall Bridge-road, London, S.W. 1.

We are, Sir, yours faithfully,

A. F. LONDON,
MANUEL J. BIDWELL,
J. SCOTT LIDGETT,
HELEN A. POWNALL
(Chairman of the Executive Committee of W.H.F.)

June 18th, 1929.

WANTED, A PHOTOGRAPH.

To the Editor of THE LANCET.

SIR,—I am forming a collection of photographs of the pioneers of tropical medicine in connexion with the museum of the new London School of Hygiene and Tropical Medicine. I am particularly anxious to secure a photograph of Dr. George Thin (1838–1903), who made notable contributions to our knowledge of tropical affections, especially in connexion with sprue. If any reader has such a portrait to spare, or would lend it to be copied it would be very much appreciated.

I am, Sir, yours faithfully,

H. B. NEWHAM, M.D.,
Curator, London School of Hygiene and Tropical Medicine.

37, Torrington-square, W.C., June 18th, 1929.

SURGICAL ILLUSTRATIONS.

To the Editor of THE LANCET.

SIR,—I cannot help feeling that your reviewer has somewhat missed the point in his note on "the Graphic Guide to Elementary Surgery," by Prof. Naegeli, an English translation of which has just appeared. (THE LANCET, May 25th, p. 1096.) Whatever its artistic merits or defects it is unquestionably the most complete attempt that has yet been made to enable the student to visualise the underlying principles of surgery. Every page of the volume is filled with thumb-nail sketches, and, although it is true that in many instances these are from the artistic standpoint extremely crude, yet in every instance they show precisely the point which the surgeon wishes to stress, so much so that it would be a perfectly simple matter for a student to revise his knowledge without ever reading a line of the text. The mere crudeness of the illustrations is in fact a guarantee that the attention of the student will be directed to the essential point and that it will not be distracted by "artistic" detail. Personally, from the point of view of a teacher, I regard the volume as a perfect gold mine of suggestions for the blackboard, for there is not a single drawing in it which cannot be reproduced in chalk in a few seconds.

In my appreciation of Prof. Naegeli's diagrams, I am speaking from experience, for in my own book, "The Art of Surgery," I have attempted to illustrate my meaning by thumb-nail sketches in a somewhat similar way, and the difficulty of doing so can only be appreciated by those who have attempted it. It has been a constant source of friendly rivalry between my artist and myself as to whether the picture should show what I want or be well drawn, and we have both realised the risk of losing the meaning of my own crude sketches in an effort after artistic perfection. It is quite obvious that Prof. Naegeli was "top dog" in the partnership, whilst I perhaps have given in too much, but I am by no means sure which of us is right. At any rate, there is no possible doubt in my mind as to the immense practical value of his book, both to the student and his teacher.

I am, Sir, yours faithfully,

Queen Anne-street, W., June 18th, 1929. H. S. SOUTTAR.

A DESERVING APPEAL.

To the Editor of THE LANCET.

SIR,—We are writing to appeal for funds on behalf of Dr. Charles Powell White, who, as the result of a severe cerebral hæmorrhage, is unable to maintain himself, his wife and family. This position is largely due to the fact that he has devoted his life to cancer research for the benefit of the general public and the world at large. By his writings and works he has obtained an international reputation as an authority on cancer problems.

For many years he has given all his time to cancer research in Manchester for the Christie Hospital for Cancer, the Pilkington Cancer Research Fund, the University of Manchester, and the Manchester Committee on Cancer. In each of these appointments he has received only a nominal salary for a man of his eminence, and not being on the teaching staff of a University, he is not eligible for any pension. Possessing the highest medical and surgical qualifications, he could have commanded a much more lucrative position in the active practice of his profession, but he preferred to use his wide knowledge of mathematics, chemistry, physics, and general natural sciences for the study of cancer, its treatment and prevention.

Dr. Powell White's work has a soundness of character and a breadth of application still only incompletely recognised. Thus it is to him that we owe the present classification of tumours—a classification which has been very widely adopted by pathologists. His other work is less generally known, since it is more mathematical and abstruse, but from it emerges the fact that certain analyses suggest that in persons suffering from malignant disease, changes occur which show that some fundamental metabolic disturbance is present in this condition and that these changes are greater than can be accounted for by the growth itself. He possesses a grip of the problem of malignant disease shared by few.

Dr. White has conducted long and tedious analyses on cancer problems which would have daunted many by their extent and difficulty, and it was in his laboratory that he was taken ill. He has a world-wide reputation as an authority on cancer, and has communicated an article on the subject to your columns. We hope that many of your readers to whom we cannot send the special letter of appeal will be able to contribute towards the fund.

Subscriptions should be sent to Mr. Wilson Hey, 16, St. John-street, Manchester.

We are, Sirs, yours faithfully,

WALTER H. MOBERLY,
Vice-Chancellor, The University of Manchester.
FREDERICK P. NATHAN,
Chairman, The Christie Pavilion and Home.
R. VEITCH CLARK,
Chairman, The Manchester Committee on Cancer.

June 18th, 1929.

LOCAL ANÆSTHESIA.

To the Editor of THE LANCET.

SIR,—The duration of anæsthesia after the injection of novocaine solution is a direct function of the concentration of the drug. It is immensely increased if adrenalin be added. This suffices to explain the long anæsthesia which Mr. C. Abbott-Brown obtains, for he uses a much stronger solution than is injected into the spinal canal and adds adrenalin which should not be used intradurally as the resulting prolonged anæmia has been thought to be harmful to the delicate nervous tissue of the spinal cord.

I am, Sir, yours faithfully,

CHARLES A. PANNETT.

Pensford-avenue, Kew Gardens, June 17th, 1929.

THE NATIONAL PHYSICAL LABORATORY.

ANNUAL INSPECTION BY THE GENERAL BOARD.

THE annual inspection of the National Physical Laboratory at Teddington by the General Board is a function to which invitations are accepted with enthusiasm. While the visitors make holiday the scientific staff are allowed to enjoy only that form of recreation which results from change of occupation, for the work of answering questions and explaining the exhibits is at least as strenuous as their ordinary labours. The problem for the visitors consisted in deciding which of over 200 exhibits they would inspect. Many of them were anxious to be towed along the William Froude national tank, and while waiting their turn found much to interest them in the moulding shop where model ships the size of small pleasure boats are cut to any desired shape by most ingenious mechanical devices. The material of which these models are made is hard wax (not, as one visitor guessed, soap) to which any desired superstructure can easily be attached.

Wind Resistance to Ships.

The tank, which is enclosed in a building, is 500 feet long, 30 feet broad, and 12 feet deep. It is used chiefly to measure the air resistance to a ship in motion by means of tests made in water. A model is made of a ship, with funnel, masts, captain's bridge, and all deck erections. This model is then inverted in the tank and so arranged that the same part of the ship is immersed as would be above the water line if the ship were floating the right way up. This model is then towed along at different angles to the direction of motion over a range of low speeds, and the resistance of the water at various points is measured by the lengthening springs on the float to which the boat is attached by wires. The object of the tests is to determine the wind resistance and centre of effort of ship superstructures, with a view to improvement in ship speed and steering.

Experiments in Acoustics.

Another direction in which experiments with water can be adapted to give useful information about air conditions is in the investigation of acoustics. The path of a ripple in water closely resembles that of a sound wave in any one plane, and a small ripple tank on the plan of a vertical section of a town or concert hall has been devised for investigating acoustic reflections. At a place corresponding to the position of a speaker in the hall a disturbance is made in the water and the wave caused and its reflections from the roof can be photographed or thrown on a screen. The hall represented has two balconies, one of which has a roof continuous with that of the main hall, and the other a roof separated from that of the main hall by a short partition extending downwards from the ceiling. One of the problems to be solved concerned the balconies. In which of them could the speaker be best heard? The answer is that unless the hall is very large the audience on the balcony with the continuous roof hear better; where, however, the total path of the sound wave after reflection is greater than the normal path by more than 75 feet, the reflection instead of intensifying the sound will cause an echo, and in a hall of these dimensions the partition is therefore desirable.

Skidding in Motor-cars.

In the engineering department the model motor-cars used in the study of skidding excited interest. They are propelled along a flat surface by a catapult; at a given distance the brakes come into operation and the deviation of the car from the straight path is recorded. Some revision of the current methods of adjusting four-wheel brakes can be anticipated as a practical outcome of these experiments. For example, the retarding force is now generally distributed by manufacturers as two-thirds on the rear wheels and one-third on the front wheels. Experiments suggest that the proportion on the front wheels should be increased. Moreover, though it is now usual for back brakes to be adjusted to lock before the front ones, the model cars are found to keep a straighter course if the front wheels lock first. The importance of keeping the centre of gravity low to avoid the risk of overturning has been shown; also the advantages of a long wheel base in preventing rotation.

The Centre of Gravity in Man.

A model figure wearing a lifebelt of the pattern officially approved was shown floating in a tank in a semi-horizontal position. A very slight adjustment, made through the hollow tube which represented his spinal column, to a small weight in this tube, served to lower this centre of gravity and he assumed the vertical posture. The efficacy of the official belt is confirmed by experiments on this model, which show, however, that the margin which may determine a fatal change of position is narrow. It is interesting to learn that the investigators found considerable difficulty in ascertaining from physiologists the normal centre of gravity of man. Eventually it was obtained from German army figures as 0·54 of his height from the feet upwards, the centre of buoyancy being very nearly the same.

The Equilibrium of Dental Amalgams.

An ambitious programme of work on dental amalgams is being pursued. The amalgams in general use are largely empirical, and are not free from disadvantages. Experiments are in progress in which amalgams of different proportions of metals—for example, silver 29 per cent., mercury 71 per cent., are heated under pressure, in order to determine the thermal critical points, and their associated dimensional changes. It is known that when the dentist has prepared his alloy and inserted it, the equilibrium of the two metals is not stable for a period still to be determined. It is important to ascertain under what conditions either contraction or expansion is to be anticipated in order that the dentist may choose the alloy most suitable to his purpose.

Colorimetric Apparatus.

The apparatus shown in connexion with the measurement of colour includes equipment arranged for determining the properties of the "normal" eye, based on measurements of the spectrum colours by a large number of observers. When this determination is completed it will form a connecting link between the various practical methods of colorimetry and the physical properties of colouring materials, and will establish an accurate standard means of recording a colour by three numbers corresponding to the amount of red, blue, and yellow of which it is composed.

Clinical Thermometers.

The department where clinical thermometers are tested has not made any important changes in technique elaborated in previous years. Since the

repeal of the law making compulsory the testing of every thermometer sold to the public, the staff has diminished to about half the number employed during the war. The standard required is not exorbitantly high—an error of less than 0·2 of a degree (Fahr.) does not lead to rejection of any thermometer. The cost to manufacturers of the test is only 3*d*. a thermometer, and if the medical profession urged the public to refrain from buying any thermometer not stamped with the letters N.P.L. at least one source of error in taking temperatures would be avoided.

Medical News.

UNIVERSITY OF OXFORD.—At a congregation on June 8th the following degrees were conferred:—

D.M.—G. I. Evans.
B.M.—R. M. J. Harper, D. C. Shields, M. V. Bhajekar, and H. G. Wells.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—A meeting of the Council was held on June 13th, with Lord Moynihan, the President, in the chair. It was announced that the Lister Medal for 1930 for distinguished contributions to surgical science had been awarded to Dr. Harvey Cushing, of Boston, U.S.A., and that Dr. Cushing had undertaken to give an address in London on some day in 1930 to be arranged later. It was also announced that the Sir Gilbert Blane Medal for 1929 had been awarded to Surgeon Lieut.-Commander T. N. D'Arcy.

Diplomas of Fellowship were conferred upon the following:—

C. D. Shapland and N. L. White, Univ. Coll.; J. C. Ainsworth-Davis, St. Bart.'s; R. C. Taylor, Univ. Coll.; E. S. Freshman, Manchester; L. N. Pyrah, Leeds and Guy's; J. V. O'Sullivan, London; A. M. Lazarus, St. Bart.'s; R. M. Bates, London; A. Simpson-Smith, Guy's; R. V. Cooke, Bristol and Guy's; H. P. Nelson, St. Bart's.; J. F. Simpson, St. Mary's; N. Attygalle, Middlesex and King's Coll.; H. J. Burrows, St. Bart.'s; G. M. FitzGibbon, St. Thomas's; Vairamuttu Kathirgamatamby, Madras, London, and King's Coll.; A. K. Gupta, London; R. W. Kenney, Dalhousie and London; F. J. Milward, St. Thomas's; N. M. Matheson, Otago and Middlesex; R. L. Flett, Otago and Guy's; S. Howard, London; M. Axford and H. S. Billcliff, Otago and Guy's; J. H. Cramsie, Sydney and St. Bart.'s; D. D. McKenzie, New Zealand and Guy's; F. E. Stabler, Durham.

Diplomas of Membership were conferred upon the following:—

Nancy M. Badeley, S. T. Crowther, Catherine Day, Margaret L. Hamburger, and L. Nallainathan.

Diplomas in Public Health were granted, jointly with the Royal College of Physicians, to the following:—

Allah Bakhsh and Y. P. Bedi, Royal Inst. of Public Health; F. G. Brown and J. P. Chaudhuri, Univ. Coll.; D. S. Chowdhary, Royal Inst. of Public Health; Gordon Covell, Guy's and Univ Coll.; S. D. De Vos, H. N. Dewan and D. P. Dutta, Royal Inst. of Public Health; Nancy G. Howell, Univ. Coll.; B. S. Kanga, Royal Inst. of Public Health; G. R. Lynn, St. Bart.'s and R.A.M. College; Elsie Lyon and D. G. Mohile, Univ. Coll.; Samuel Mufty, Royal Inst. of Public Health; C. C. Po, Univ. Coll.; Marion Ravell, A. E. Schokman, Amarnath Sharma, Patricia H. S. Shaw, and K. A. Soutar, Royal Inst. of Public Health; H. S. C. Starkey, St. Bart.'s; G. G. Stewart, St. Bart.'s and Middlesex; K. M. R. Swami, J. P. R. Tennekoon, and R. L. Tull, Royal Inst. of Public Health.

At the primary examination for the Fellowship, held from June 4th to 14th, for which 164 candidates presented themselves, 47 were approved. The following are the names and schools of the successful candidates:—

A. H. Baker, M.B., Manchester; D. S. M. Barlow, M.B., Middlesex and St. Mary's; A. W. Bayley, M.B., Melbourne and Univ. Coll; K. B. Bridge, M.B., Otago; E. Carew-Shaw, M.R.C.S., King's Coll.; D. O. Clark, St. Thomas's; A. A. Davis, M.B., Manchester and Middlesex; E. A. Devenish, Univ. Coll.; K. J. Elliott, Edinburgh and Middlesex; A. L. Eyre-Brook, Bristol; L. Fatti, M.B., Univ. Coll.; K. Fletcher-Barrett, M.B., Cambridge and St. George's; R. J. Furlong, St. Thomas's; J. Gabe, M.B., St. Mary's and Middlesex; R. H. Hadley, M.B., Melbourne and Middlesex; C. S. Hallpike, M.R.C.P., Guy's and King's Coll.; J. Hardman, Birmingham; E. A. H. Hindhaugh, M.R.C.S., Univ. Coll.; O. Hooper, B.M., Oxford and London; Ruby D. Johnson, Oxford and Univ. Coll.; E. C. B. Jones, M.B., Melbourne and London; H. Y. Khwaja, M.B., Bombay and London; C. E. Kindersley, M.B., St. Bart.'s and St. Mary's; S. Lal, M.B., Punjab and Middlesex; M. Lee, M.B., Durham and Middlesex; M. J. F. McArdle, Guy's; D. J. MacMyn, M.B., Cambridge and King's Coll.; D. H. Mitchell, M.B., Melbourne and King's Coll.; E. W. T. Morris, M.R.C.S., Adelaide and St. Thomas's; A. B. Pain, M.B., Leeds; G. T. Partridge, Camb. and St. Bart.'s; R. S. Pilcher, M.R.C.S., Univ. Coll.; A. E. Porritt, M.B., Otago and St. Mary's; C. A. M. Renou, M.B., Melbourne and Middlesex; L. A. Riddell, M.B., Otago and St. Mary's; T. O. Sayle, M.B., Melbourne and Middlesex; H. H. Skeoch, M.B., Sydney and King's Coll.; J. O. Smith, M.D., Melbourne and Middlesex; S. B. Smith, Guy's; F. R. Stansfield, M.B., Leeds; S. C. Suggit, Univ. Coll.; B. M. Sundaravadanam, M.B., Madras and London; G. L. Talwar, Punjab and St. Thomas's; K. H. Watkins, M.B., Manchester and Middlesex; F. E. Webster, M.B., Otago; Eileen M. Whapham, Lond. Sch. Medicine for Women; H. L. C. Wood, M.B., King's Coll.

The following examiners were elected for the ensuing year:—

Dental Surgery.—(Surgical Section).—Mr. L. Bathe Rawling, Mr. H. S. Clogg, Mr. T. P. Legg, Mr. Russell J. Howard, Mr. Gwynne Williams, Mr. John Murray, Sir Cuthbert Wallace, and Mr. Clement E. Shattock.
Primary Fellowship.—(Anatomy).—Mr. C. P. G. Wakeley, Mr. P. N. Blake Odgers, Prof. William Wright, and Prof. J. E. Frazer; (Physiology)—Prof. H. E. Roaf, Prof. C. Lovatt Evans, Prof. R. J. S. McDowall, and Prof. John Mellanby.
Conjoint Qualification.—(Elementary Biology).—Dr. T. W. Shore and Prof. J. P. Hill; (Anatomy)—Mr. J. Basil Hume, Prof. William Wright, and Mr. R. Bramble Green; (Physiology)—Prof. E. B. Verney and Prof. Hamilton Hartridge; (Midwifery)—Mr. Clifford White, Mr. T. Berwyn Davies, Mr. Aleck W. Bourne, and Mr. Sidney Forsdike.
Diploma in Public Health.—Dr. C. W. Hutt.
Diploma in Tropical Medicine and Hygiene.—Colonel W. P. MacArthur and Dr. P. H. Manson-Bahr.
Diploma in Ophthalmic Medicine and Surgery.—Mr. C. B. Goulden, Mr. H. Willoughby Lyle, and Mr. R. Affleck Greeves.
Diploma in Psychological Medicine.—Dr. F. L. Golla.
Diploma in Laryngology and Otology.—Mr. W. M. Mollison, Mr. Norman Patterson, and Mr. Walter G. Howarth.

Mr. W. McAdam Eccles was appointed the representative of the College on the British Social Hygiene Council in place of the late Sir Anthony Bowlby.

UNIVERSITY OF BRISTOL.—At recent examinations the following candidates were successful:—

FINAL EXAMINATION FOR M.B., CH.B.

Part I. Forensic Medicine and Toxicology only.—A. J. B. Miall, H. M. Strover, and W. L. Sleight.
Part II. *R. A. S. Cory, *R. J. Krogh, Isabella J. Armstrong, A. C. Fisher, and April D. James.
Part II. (Group I.).—N. D. Gerrish and Mabel F. Potter.
Part II. (Group II.).—N. L. Price and †Eric Southam.
* With Second Class Honours. † Completing examination.

FINAL EXAMINATION FOR L.D.S.

C. R. H. Edwards and L. W. G. Jones.

THE Parliamentary Secretary to the Ministry of Health, Miss Susan Lawrence, M.P., has appointed Mr. D. C. L. Ward to be her private secretary.

A MOTORISTS' HOSPITAL BADGE.—A Motorists' Fund has been opened in aid of Nottingham General Hospital. In return for an annual payment of 10*s*. for a private car, 5*s*. for a commercial vehicle, and 2*s*. 6*d*. for a motor-cycle the owner receives a badge which can be fixed to the vehicle. There are nearly 14,000 motor drivers in the City of Nottingham, and last year 40 persons were killed and 987 injured in vehicular street accidents.

POST-GRADUATE COURSE AT TRINITY COLLEGE, DUBLIN.—The authorities of the School of Physic, Trinity College, Dublin, have issued the prospectus of their annual post-graduate course, which will begin on Sept. 16th, and last for three weeks. The lectures and demonstrations range over medicine, surgery, and midwifery, with the ancillary specialties, and the teachers include many of the leading specialists in Dublin, as well as the staff of the school. An attractive feature of the course is that members of the class can be housed and boarded in Trinity College on moderate terms, while women members can be accommodated at Trinity Hall.

OXFORD OPHTHALMOLOGICAL CONGRESS.—As we have already announced, this Congress will be held at Keble College, Oxford, from Thursday, July 4th, to Saturday, the 6th. On Thursday, at 10 A.M., the proceedings will begin with an address by the Master, Mr. Bernard Cridland, after which a discussion on diseases of the lacrymal apparatus will be opened by Prof. Joseph Meller, of Vienna, and Dr. J. S. Fraser, of Edinburgh. After lunch there will be demonstrations in the Scientific and Commercial Museums, and in the evening the annual dinner of the Congress will be held at Keble College. On Friday, at 11 A.M., Miss Ida Mann will deliver the Doyne Memorial Lecture, entitled Some Observations on the Vascularisation of the Vertebrate Eye, and at 3 P.M. Mr. Hugh Cairns and Mr. Charles Goulden will open a discussion on the Ocular Manifestations found in Head Injuries. Saturday morning will be devoted to shorter addresses. Further particulars may be had from the hon. secretary of the Congress, Mr. C. G. Russ Wood, 12, St. John's Hill, Shrewsbury.

NORTH-EAST COAST EXHIBITION.—The attention of medical men visiting this exhibition is drawn to the accommodation and facilities offered by the Medical Institute, 7, Windsor-terrace, Newcastle-upon-Tyne.

EXTENSION OF ACTON HOSPITAL.—Last week Lady Skinner opened an extension of Acton (Middlesex) Hospital. The enlargement comprises a nurses' home, private wards, and administrative offices.

SOUTH LONDON HOSPITAL FOR WOMEN.—A house-to-house collection in Clapham has produced £1000 for the endowment of this hospital on Clapham Common, and recently Princess Helena Victoria, the President, unveiled a commemorative tablet at the head of the bed. The new out-patient's block has cost £65,000, and £28,000 is required to enable it to be opened free of debt.

UNIVERSITY OF MANCHESTER.—The University Council have appointed Dr. Frank Edward Tylecote to be Professor of Systematic Medicine as from Sept. 29th.

Dr. Tylecote was a student in the Manchester Medical School and graduated as M.B. in 1902 and M.D. in 1904. He has been honorary physician to the Manchester Royal Infirmary since 1914, in which year he resigned his appointment as senior honorary physician to the Salford Royal Hospital. Last year he was the chairman of the Medical Board of the Manchester Royal Infirmary. From 1914–19 he held a commission in the Royal Army Medical Corps (T.F.), and attained the rank of major on the staff of the 57th General Hospital, British Expeditionary Force. He has been a lecturer in clinical medicine in the University of Manchester since 1916, and was elected Fellow of the Royal College of Physicians of London in 1923.

ST. THOMAS'S HOSPITAL.—Speaking at the annual distribution of Medical School prizes by the Duke of Connaught at St. Thomas's Hospital last week, Sir Arthur Stanley, the treasurer, explained a change of plans respecting the proposed new Medical School. Instead of building a new out-patients' department on the opposite side of Lambeth Palace-road, as originally intended, it had been decided, for reasons of convenience, to transfer the school to the new site and to transform the existing school into an enlarged out-patients' department. The present accommodation for these patients is totally insufficient. When the hospital was built in 1871 there were 60,000 attendances; last year there were 601,000. There is also urgent need for an enlarged nursing home for middle-class patients, and a site in Paris-street adjoining that of the new Medical School has been secured. The present St. Thomas's Home has 40 beds, always full, and 80 or 100 could be filled.

ST. THOMAS'S HOSPITAL DINNER.—The annual dinner of old students will be held at St. Thomas's House, Lambeth Palace-road, London, S.E., on Friday, Oct. 4th, with Dr. H. G. Turney in the chair.

HARVEIAN SOCIETY OF LONDON.—The annual dinner of this Society which was held at the Connaught Rooms on June 13th was something of a red-letter day owing to the approach of a centenary celebration and the presence of Mr. G. Buckston Browne, the doyen of the Society. Guests had the opportunity of seeing and examining for themselves a new portrait of Harvey discovered by Dr. C. M. Wilson. Mr. Duncan Fitzwilliams, who occupied the chair, in recalling the aim of the Society to initiate discussion of clinical medicine in its broadest aspect, remarked that Harvey was as much a surgeon as a physician, and one who, like Hunter after him, dissected every imaginable kind of animal. His own particular ambition was to secure publication of the discussions in the form of transactions which could be circulated to the whole medical profession. Sir D'Arcy Power, in proposing "The Society," remarked on its highly hereditary character, for he had himself been its secretary 40 years ago, and was the son of a former President, while his neighbour, Sir John Broadbent, was the son of another. The toast of "The Visitors" was proposed by Dr. R. Cove-Smith in a cheerfully provocative vein. Besides those who were to respond, they welcomed at the dinner the Presidents of the other independent medical societies in London, as well as the medical heads of the Navy and of the Air Force. Response was made by Dr. J. Walter Carr, who offered the thrilling suggestion of a guest who had the audacity to refuse when asked to reply: by Lieut.-Colonel C. T. Samman, Master of the Society of Apothecaries; and by Mr. A. P. Herbert, who as a member of the staff of *Punch* described himself as the only Christian among a tribe of cannibals, and one of the few present with a real faith in the medical profession. It was, he said, the only department in public life that had a firm conviction it was making progress. During the evening Mr. Finlay Dunn rendered some amusing skits at the piano with acclamation. The officers of the Society could not be induced to speak for themselves, but due acknowledgment was made to Dr. G. de Bec Turtle, Dr. J. A. B. Hammond, and Dr. H. C. Bull of their share in a happy and well-arranged festivity.

Medical Diary.

SOCIETIES.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.
THURSDAY.—UROLOGY: Summer Meeting, 11 A.M. to 1 P.M. Exhibition of Urological Instruments. 2 P.M., Operations at St. Peter's Hospital, Henrietta-street, W.C. 8.30 P.M., Sir John Thomson-Walker Cinematographic demonstration showing a prostatectomy, litholapaxy and internal urethrotomy.

MEDICO-LEGAL SOCIETY.
THURSDAY, June 27th (at 11, Chandos-street, Cavendish-square, W.), At the conclusion of the Annual General Meeting a Paper will be read by Dr. Francis Temple Grey on The Medico-Legal Expert in France, followed by a discussion.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY.
WEDNESDAY, June 26th.—4.15 P.M., (at St. John's Hospital, 49, Leicester-square, W.C.), Annual General Meeting followed by Clinical Cases.

TUBERCULOSIS ASSOCIATION.
THURSDAY, June 27th, to SATURDAY, the 29th.—Provincial Meeting at Medical School, Cambridge.

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, W.
MONDAY, June 24th to SATURDAY, June 29th.—MEDICAL SOCIETY OF LONDON, 11, Chandos-street, Cavendish-square, W. M.R.C.P. Course of Lectures, on Tues. and Fris. at 8.30 P.M. Tues., Dr. Harold Pritchard: Diseases of the Pancreas. Fri., Dr. A. F. Tredgold: Mental Deficiency.—HOSPITAL FOR EPILEPSY AND PARALYSIS, Maida Vale, W. Thurs. at 2.30 P.M., Lecture-demonstrations by Dr. W. G. Wyllie on Nervous Disease in Children. No fee.—CENTRAL LONDON THROAT, NOSE AND EAR HOSPITAL, Gray's Inn-road, W.C. Thurs. at 2 P.M., Mr. Harold Kisch: Clinical demonstration in the O.P. Department. No fee. ST. MARK'S HOSPITAL, City-road, E.C. All-day Course in Proctology, lectures, demonstrations, operations. One week only.—CHILDREN'S CLINIC and other Hospitals. Special two weeks' course in Diseases of Children, occupying most afternoons and some mornings.—PRINCE OF WALES'S GENERAL HOSPITAL, Tottenham, N. Special post-graduate course in medicine, surgery, and the special departments, for two weeks from 10.30 A.M. to 5.30 P.M. daily.—Further particulars from the Fellowship of Medicine.

NORTH-EAST LONDON POST-GRADUATE COLLEGE, Prince of Wales's General Hospital, Tottenham, N.
MONDAY, June 24th.—2.30 to 5 P.M., Medical, Surgical, and Gynæcological Clinics. Operations.
TUESDAY.—2.30 to 5 P.M., Medical, Surgical, Ear, Nose and Throat Clinics. Operations.
WEDNESDAY.—2.30 to 5 P.M., Medical, Skin, and Eye Clinics. Operations.
THURSDAY.—11.30 A.M., Dental Clinics. 2.30 to 5 P.M., Medical, Surgical, Nose, Throat and Ear Clinics. Operations.
FRIDAY.—10.30 A.M., Throat, Nose and Ear Clinics. 2.30 to 5 P.M., Surgical, Medical, and Children's Diseases Clinics. Operations.

WEST LONDON HOSPITAL POST-GRADUATE COLLEGE, Hammersmith, W.
MONDAY, June 24th.—10 A.M., Dr. Dowling: Skin Department. 11 A.M., Mr. Tyrrell Gray: Ward Visit. 2 P.M., Mr. Donald Armour: Operations.
TUESDAY.—10 A.M., Medical Registrar: Ward Visit. 2 P.M., Mr. Addison: Operations. 2 P.M., Mr. Sinclair: Surgical Out-patients.
WEDNESDAY.—10 A.M., Dr. Owen: Children's Out-patient Department. 2 P.M., Mr. Tyrrell Gray: Operations. 2 P.M., Dr. Scott Pinchin: Medical Out-patients.
THURSDAY.—10 A.M., Dr. Grainger Stewart: Neurological Department. 11.30 A.M., Mr. Simmonds: Demonstration of Fractures. 2 P.M., Mr. MacDonald: Genito-Urinary Out-patient Department.
FRIDAY.—10 A.M., Dr. Pritchard: Medical Ward Visit. 12 noon, Dr. Shaw: Clinical Demonstration. 2 P.M., Mr. Vlasto: Throat, Nose and Ear Department.
SATURDAY.—9.30 A.M., Dr. Burnford: Bacterial Therapy Department. 10 A.M., Dr. Owen: Children's Medical Out-patient Department. 10 A.M., Resident Assistant Surgeon: Ward Visit. Medical and Surgical Out-patients at 2 P.M., daily. Operations. Special Departments daily, 10 A.M. to 5 P.M., Saturdays 10 A.M. to 1 P.M. Special Classes in Anæsthetics and Operative Surgery.

NATIONAL HOSPITAL, Queen-square, Bloomsbury, W.C.
MONDAY, June 24th.—2 P.M., Dr. Riddoch: Out-patient Clinic. 3.30 P.M., Dr. Collier: Poliomyelitis.
TUESDAY.—2 P.M., Dr. Walshe: Out-patient Clinic. 3.30 P.M., Dr. Grainger Stewart: Post-traumatic Neuroses (2).
THURSDAY.—2 P.M., Dr. Kinnier Wilson: Out-patient Clinic. 3.30 P.M., Mr. Just: Demonstration of Methods of Testing the Eighth Nerve.
FRIDAY.—2 P.M., Dr. Adie: Out-patient Clinic. 3.30 P.M., Dr. Walshe: Spastic Paralysis.

ST. PAUL'S HOSPITAL, Endell-street, W.C.
THURSDAY, June 27th.—4.30 P.M., Mr. W. K. Irwin: The Diagnosis and Treatment of Some Important Bladder Conditions.

NATIONAL CAMPAIGN AGAINST RHEUMATIC DISEASES.

WEDNESDAY, June 26th.—5 P.M. (at the Royal Society of Medicine, 1, Wimpole-street, W.). Meeting of supporters. (Chairman: Sir Thomas Horder.)

Appointments.

ALEXANDER, B., M.D., C.M., has been appointed Resident Surgical Officer at the Manchester Royal Eye Hospital.

BROOKFIELD, R. W., M.D., Ch.B. Liverp., D.P.H., Hon. M.O., Royal Southern Hospital, Liverpool.

LITTLE, R. C., M.B., Ch.B. Edin., Certifying Surgeon under the Factory and Workshop Acts for Witham, Essex.

RAE, HARRY J., D.S.O., M.B. Aberd., D.P.H., Medical Officer of Health for City of Aberdeen.

Manchester Royal Infirmary: MELLAND, C. H., M.D., F.R.C.P. Lond., Hon. Physician; and FERGUSON, F. R., M.D. Manch., D.P.H., Hon. Asst. Physician.

New Sussex Hospital for Women and Children, Brighton: NEATE, DOROTHY L., M.B., B.S. Lond., House Physician; BISSET, SUSAN, M.B., Ch.B., House Surgeon.

Vacancies.

For further information refer to the advertisement columns.

Bath, Royal United Hospital.—Asst. H.S. At rate of £100.

Belgrave Hospital for Children, 1, Clapham-road, S.W.—Asst. P. 50 gns.

Birmingham, Dudley-road Hospital.—Jun. Asst. M.O.'s. Each at rate of £200.

Birmingham General Hospital.—Res. Surg. Reg., &c. £100–£140. Two Res. Anæsthetists. Each £120. Also three H.P.'s. Each £70.

Bolton Infirmary and Dispensary.—H.S. At rate of £150.

Bootle Borough Hospital, Derby-road.—Sen. M.O. Also Two Jun. M.O.'s. At rate of £150 and £125 respectively.

Bradford, Royal Eye and Ear Hospital.—Jun. H.S. £120.

Brighton, Royal Sussex County Hospital.—Two Cas. H.S.'s. Each £120.

Bristol City Mental Hospital.—Third Asst. M.O. £350.

Central London Ophthalmic Hospital, Judd-street, St. Pancras, W.C.—Sen. and Jun. H.S. £120 and £100 respectively.

Central London Throat, Nose and Ear Hospital, Gray's Inn-road, W.C.—Asst. S. Two Chief Clin. Assts. Also Res. H.S. At rate of £75.

Chester Royal Infirmary.—H.S. to Ear, Nose and Throat Dept. and Cas. O. £120. Also H.S. £120.

Derby, Guardian's Institution and Infirmary.—Second Res. M.O. £250.

Dublin, Dr. Steevens Hospital.—Resident Surgeon. £150.

Dudley, Guest Hospital.—Hon. Orthopædic Surgeon. Also H.S. and Asst. H.S. £175 and £150 respectively.

Durham County Council.—Asst. Welfare M.O. £600.

East Suffolk Administrative County.—Asst. County M.O. £625.

East Suffolk, Administrative County of.—Asst. County M.O.H. £600.

Essex, Administrative County of.—Asst. County M.O.H. £600.

Evelina Hospital for Children, Southwark, S.E.—H.P. At rate of £120.

Exeter, Devon Mental Hosp., Exminster.—Jun. Asst. M.O. £300.

Exeter, Royal Devon and Exeter Hospital.—Asst. H.S. At rate of £100.

Farringdon General Dispensary, Holborn-circus, E.C.—Hon. Surgeon to Dental Department.

Gateshead County Borough, Mental Hospital, Stannington.—Asst. M.O. £400.

General Lying-in Hospital, York-road, Lambeth, S.E.—Hon. Asst. P.

Gloucester, Gloucestershire Royal Infirmary.—H.P. At rate of £150.

Golden-square, Throat, Nose and Ear Hospital, W.—Hon. Asst. S.

Grange-over-Sands, Westmorland Sanatorium, Meathop.—Med. Supt. £800.

Great Yarmouth General Hospital.—Jun. H.S. £100.

Hellingly, East Sussex County Mental Hospital.—Res. Locum Tenens M.O. 7 guineas per week.

Hosp. for Sick Children, Great Ormond-st., W.C.—Part-time Jun. Cas. O. At rate of £150. Also Res. M.O. for Country Branch Hospital, Tadworth Court, Tadworth, Surrey. At rate of £250.

Hull Royal Infirmary.—2nd Res. H.S., Res. H.S. to Ophth Dept., &c. Each at rate of £150. Also Res. Cas. H.O. At rate of £130.

Ilford Emergency Hospital.—Jun. H.S. £100.

Indian Medical Service.—Recruitment of European Officers.

Ipswich County Borough Sanatorium.—Asst. M.O. At rate of £250.

Ipswich, East Suffolk and Ipswich Hospital.—H.S. At rate of £120.

Leeds, St. James' Hospital.—H.P. and S. £200.

Leicester Royal Infirmary.—M.O. for V.D. Dept. £4 10s. per week.

Liverpool, David Lewis Northern Hospital.—Surgical Tutor. £145.

Liverpool Eye and Ear Infirmary, Myrtle-street.—H.S. to Ophthalmic Dept. £100.

Liverpool Heart Hospital.—Maurice Stern Research Fellowship. £150.

Liverpool University.—Jun. Lecturer. £300.

London, Administrative County of.—Principal M.O.H. to Pub. Health Department. £2000.

London Temperance Hospital, Hampstead-road, N.W.—Cas. O. At rate of £120.

Lowestoft and North Suffolk Hospital.—H.S. £120.

Macclesfield General Infirmary.—Res. H.S. £180.

Manchester University.—Amy Henrietta Worswick Fellowship. £150.

M.A.B. Mental Hospitals Service.—Jun. Asst. M.O. £500.

M.A.B. Tuberculosis Service.—Consulting Laryngologist. At rate of 200 guineas.

Miller General Hospital, Greenwich-road, S.E.—H.P., H.S. Each at rate of £125. Also Pathologist. £600.

Nottingham General Hospital.—Res. Surgeon. £250.

Palestine, Hebron Medical Mission.—Medical Missionary.

Poplar Hospital for Accidents, East India Dock-road, Poplar, E. 2nd Res. O. At rate of £175.

Preston Union.—Jun. Res. M.O. At rate of £104.

Prince of Wales's General Hospital, Tottenham, N.—Hon. Asst. S. to Ear, Nose and Throat Dept.

Princess Louise Kensington Hospital for Children, N. Kensington.—H.S. At rate of £75–£100.

Queen Mary's Hospital for the East End, E.—Hon. M.O. for Electro-Therapeutic Dept. Hon. S. for Orthopædic Dept. Hon. P. for Skin Dept. Anæsthetist. 50 guineas. Also Cas. O. £150.

Queen's Hospital for Children, Hackney-road, E.—Surgeon to Ear, Nose and Throat Dept.

Rochester, St. Bartholomew's Hospital.—Third Res. M.O. At rate of £175.

St. Bartholomew's Hospital.—Asst. Physician and Asst. Director of the Medical Professorial Clinic.

Sheffield City Hospitals.—Res. M.O. £350.

Sheffield, Jessop Hospital for Women.—Three Asst. H.S.'s. Each at rate of £100.

Shrewsbury, Royal Salop Infirmary.—Res. Surg. O. £200.

Stafford, Staffordshire General Infirmary.—H.S. Also H.P. At rate of £200 and £150 respectively.

Stockport Infirmary.—Asst. Aural Surgeon for Ear, Nose and Throat Dept.

Surrey County Council.—Asst. M.O. £600.

Swansea County Borough.—Asst. M.O. £600.

Swansea Hospital.—Res. H.P. £150 to £200. Also Res. H.S. £150.

Truro, Royal Cornwall Infirmary.—H.S. £170.

Tunbridge Wells, Eye and Ear Hospital.—H.S. £150.

University of London.—External Examinerships.

Victoria Hospital for Children, Tite-street, Chelsea, S.W.—H.S. At rate of £100.

Walsall and West Bromwich Union, Great Barr Park Institution. Asst. M.O. £200.

Watford, Herts, Peace Memorial Hospital.—Res. M.O. At rate of £150.

West London Hospital, Hammersmith, W.—Director to Venereal Dis. Dept. £700.

Western Ophthalmic Hospital, Marylebone-road, N.W.—Sen. Non.-Res. H.S. At rate of £150.

Weston-Super-Mare Urban District.—Part-time M.O.H. £600.

Willesden General Hospital, N.W.—Res. H.S. At rate of £100.

Wolverhampton Royal Hospital.—Two Surgeons to Ear, Throat and Nose Dept.

Wrexham and East Denbighshire War Memorial Hospital.—Two Res. H.S.'s. Each at rate of £150.

York County Hosp.—H.S. Also Res. Anæsthetist. Each £150.

The Chief Inspector of Factories announces a vacancy for a Certifying Factory Surgeon at Chapel-en-le-Firth (Derbyshire).

Births, Marriages, and Deaths.

BIRTHS.

BYWORTH.—On June 4th, at Savernake, Stanmore, the wife of Dr. Harold A. Byworth, of a daughter.

GILLESPIE.—On June 10th, at a nursing home, Headingley, the widow of Dr. R. K. H. Gillespie, of Headingley, Leeds, of a daughter.

PRIDHAM.—On June 7th, at Hillfield, Broadway, Weymouth, the wife of Dr. J. A. Pridham, of a daughter.

SPACKMAN.—On June 4th, at Coventry-road, Market Harborough, the wife of Dr. E. D. Spackman, of a son.

THOMSON.—On June 9th, at Overstrand Mansions, S.W., the wife of Ian S. Thomson, M.D., of a son.

TRAILL.—On June 7th, at Ottery St. Mary, the wife of R. R. Traill, M.B., B.Ch., of a daughter.

WHITEHEAD.—On June 16th, at Woodfield, Cheadle Hulme, to the wife of Gordon Whitehead, M.B., Ch.B.—a son.

WILSHERE.—On June 6th, the wife of Roger G. Wilshere, L.D.S., Sunrise, Grovelands-road, Purley, of a daughter.

MARRIAGES.

MORGAN—THOMAS.—On June 12th, at Tredergarville Church, Cardiff, T. W. Morgan, M.R.C.S., L.R.C.P., to Dorothy, elder daughter of Mr. and Mrs. Edward Thomas, 7, Winchester Avenue, Cardiff.

DEATHS.

BRAND.—On June 11th, at Bellfield, Banchory, William Henry Eden Brand, F.R.C.S.E., D.P.H.

FAWSSETT.—On June 17th, at High-street, Lewes, Frank Fawssett, M.B., B.S. Lond., M.B.E., aged 64.

FRAZER.—On June 13th, at Upton Lodge, Eastbourne, Kenneth Frazer, M.D., aged 71.

JOLLYE.—On June 3rd, at Brooklands, Hemel Hempstead, Herts, Arthur Dixon Jollye, M.D., aged 57 years.

TRESIDDER.—On June 13th, at The Waldrons, Croydon, the residence of his sister, William Elliott Tresidder, M.B., B.S. Lond., aged 65.

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages, and Deaths.

Notes, Comments, and Abstracts.

HEALTH OF BECHUANALAND.

In the annual report on the affairs of this Protectorate, signed by Mr. C. L. O'B. Dutton, Government Secretary, it is stated that health conditions during the year ended March 31st, 1928, have been, as regards widespread prevalence of disease, the worst for the past ten years. During the winter of 1927, which ushered in a series of severe outbreaks of fever, following upon cold snaps, the incidence of disease was little less favourable than what is usual at that date. But with the opening and advance of summer there was a sudden rise in the prevalence of fever, which continued to increase until during January, February, and March it had assumed epidemic form and prostrated thousands of the native population. The epidemic was chiefly confined to the southern portions of the Protectorate —especially the alluvial levels—the valleys and low-lying granitic areas, abutting on the main watersheds—Molepolole, Mochudi, Gaberones, Ramoutsa, and Gopane.

Associated with this extensive prevalence of malaria were the invariable complications of influenza and bronchial catarrhs—bronchitis, acute pneumonia, rheumatic affections, enteritis, and the common sequelæ. The total returns of disease, which are the heaviest on record (close upon 20,000 cases), have been swelled to these unusual proportions by the record of many ailments, concurrent and otherwise, which the increased medical activities in connexion with the epidemic brought under observation.

Free Government supplies of quinine were issued to the areas most severely affected. And this, together with measures of supervision of distribution and energetic medical attention, helped to mitigate the effects of this disease. A fortunate and remarkable feature of the epidemic was the low rate of mortality. At Mochudi, where over a thousand cases of malaria were seen, there were only two deaths, and these of indirect or remote connexion. At Gaberones, Molepolole, Ramoutsa, and Gopane, where the numbers were still greater, the death-rate was equally low in proportion. The epidemic outbreaks were largely determined by the conditions prevailing over the southern Protectorate throughout the summer—that is, heavy rains at long intervals, over the impervious, low-lying, and easily water-logged areas; the constitutional lack of stamina of the people on the low-lying lands as against those on the higher levels—which is a long observed and constant factor—invariably shows up under unusual meteorological conditions, such as heavy rains or severe cold snaps.

Of other epidemic and infectious diseases the returns for the year show: anthrax 15 cases (1 death); dysentery, infantile or undefined diarrhœas, 627 cases; influenza, 257 cases; tuberculosis, 142 cases; puerperal fever, 2 cases; leprosy, 16 cases; enteric fever, 8 cases (1 death); tetanus, 2 cases (1 death); cerebro-spinal meningitis, 5 cases; scarlet fever, 1 case; measles, 13 cases; and a few cases of whooping-cough, mumps, and chicken-pox. The tuberculous cases generally gave a history connecting the origin of the disease with working on the Rand mines, whilst the unusual outbreaks of enteric fever were clearly traced to the Lichlenburg diamond diggings. There has been an increase in the number of syphilitics treated, the returns for the various districts showing an aggregate of 4782 attendances.

During the month of November water was struck on the site selected for the Serowe Hospital. Subsequent tests have proved the supply to be ample, and as the bedrock is pure sandstone, the supply is not likely to vary or be affected by drought. The work of clearing the site and fixing the position of the hospital and accessory buildings has since been put in hand, the hospital plans reviewed and adopted in final form, and it is intended that the new hospital shall be finished, equipped, and staffed during the next financial year.

The position with regard to the extension of plague and the proximity to the Protectorate borders of suspected and proved infection gave cause for increased vigilance, and at the end of the financial year measures were under consideration for taking practical steps, during the coming summer, towards conducting a rodent-infected survey of the Protectorate along the boundaries of possible approach.

The territory of the Bechuanaland Protectorate is bounded on the south and east by the Union of South Africa, on the north-east by Southern Rhodesia, on the north and on west by the territory of South-west Africa. It has not been surveyed as a whole, but its area is estimated at 275,000 square miles. Its mean altitude is about 3300 ft.

A CASE OF ENURESIS.

To the Editor of THE LANCET.

SIR,—In reply to "Puzzled," when I meet such a case as this I give a suitable gland compound: if the patient is cured, I am right, if not, no harm is done. Generally some good results. Using thyroid gland alone, I have had at times to stop it, as unpleasant symptoms arose, but this has never occurred with a gland *compound* tablet, such as Dynotabs Thygon-Spermin, 106 (to be obtained from Hormones and Chalones, 27, Cavendish-square, W.1). I offer the suggestion that if the system needs a gland extractit absorbs it; if it is not required it is simply passed out by some safety valve.

I am, Sir, yours faithfully,

C. G. S. BARONSFEATHER, M.D.

Bournemouth, June 15th, 1929.

CARE AND TREATMENT OF THE PATIENT.

Dr. Emerson has brought together here nine essays[1] by well-known American authorities, the origin of the work being the establishment of a set of lectures in the Harvard Medical School dealing with the personal care of the patient by the physician. The following well-known teachers have contributed to the volume: Dr. David L. Edsall, Dr. C. F. Martin, Dr. W. S. Thayer, Dr. Austen Fox Riggs, Dr. Franklin G. Balch, Dr. Lawrence K. Lunt, and Dr. Alfred Worcester. One of the most useful essays is entitled "The Medical Education of Jones by Smith," and purports to be introduced by Dr. Thayer. The characters may be imaginary but the precepts have the ring of being founded upon reality. Whether "Smith" is "Jones," whether either is Prof. Thayer, and who was "Fowler" are questions the answers to which could probably be provided at Harvard, but the personalities have no significance, which is exactly what the teaching possesses. It is interesting to read Dr. Alfred Worcester's chapter on the care of the aged alongside the section in Dr. David Tindal's book on the treatment of the aged (see below) for the obviously learned American and the delightfully simple Englishman provide sensible teaching between them, each supplying notes that are lacking in the pages of the other.

Dr Tindal[2] has set down in his "Gleanings from General Practice" the results of long experience as an urban practitioner, in the hope that they may prove of service to young members of the profession. We may say at once that his gleanings are useful while his advice is sound. Wise remarks on professional conduct, some of which are so obvious that they are perhaps needless, lead to chapters on treatment generally, treatment of children and of the aged, and where, as not infrequently happens, part of the treatment is connected with diet, reference is given to a useful section of the book containing notes on cookery and the serving of meals in the sick-room. The last 50 pages of the book are taken up with formulæ, the prescriptions being directed generally or specially towards the relief of common conditions. Certain preliminary reflections of the author, which point to the absence of instruction given to-day to students in regard to the conduct of practice, justify the issue of this unpretentious work.

PHARMACEUTICAL LATIN.

A COMPACT little book,[3] measuring only 6¼ by 4 inches, provides the pharmaceutical and medical student with a concise Latin grammar and a list of phrases and abbreviations used in prescriptions, a few exercises and examples of prescriptions, and a Latin-English vocabulary. After absorbing its contents the student should be well primed. He will note that O.o.o. stands for the best olive oil (oleum olivæ optimum) and that S.o.S. to a pharmacist is a call for help only if there is need (si opus sit). M.d. means as directed (more dicto) and M.p. is a pill mass. The reaction of a grocer to the precious student who asks for pastilles as "coni odorati" or for a packet of isinglass as "colla piscium" might be alarming. Incidentally, for isinglass most dictionaries prefer the Greek "ichthyocolla." "Cascara sagrada," which is included in the Latin-English vocabulary and explained as cascara, bark, sagrada, adj. sacred, is really pure Spanish, except that the first a has an accent in that language. The word cortex, bark, is included in its proper place. Vehiculum is described as vehicle. The explanation might have been extended by adding "excipient or medium." Ne tr. s. num. (ne tradas sine nummo) seems to be the druggist's way of saying what other tradesmen more simply call "C.o.d.", but then the druggist keeps a "taberna" and not a shop. The book will be useful especially to students near qualification whose powers of writing prescriptions are too often limited to a quotation of the name of the mixture in the Hospital Pharmacopœia deemed most nearly appropriate to the patient's condition.

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[1] Physician and Patient: Personal Care. Edited by L. Eugene Emerson. Harvard University Press. London: Humphrey Milford, Oxford University Press. 1929. Pp. 244. 11s. 6d.

[2] Gleanings from General Practice. By David Tindal, M.D., F.R.F.P.S. Glasg. London: Baillière, Tindall and Cox. 1929. Pp. 209. 6s.

[3] Aids to Pharmaceutical Latin. By G. E. Trease, Ph.C., Lecturer in Pharmacognosy, University College, Nottingham. London: Baillière, Tindall and Cox. 1929. Pp. 108. 3s. 6d.